# ORIENTATION BEHAVIOUR OF DROSOPHILA MELANOGASTER

DISSERTATION
zur Erlangung des Grades eines Doktors
der Naturwissenschaften

der Fakultät für Biologie
der Eberhard - Karls - Universität Tübingen

vorgelegt von
HEINRICH BÜLTHOFF
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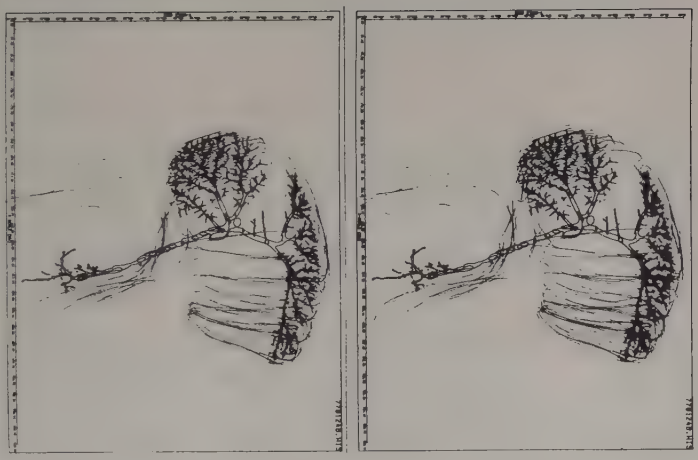
# PART 1

# 3-D Analysis



VS1 cell of the lobula plate of Calliphora
reconstructed in collaboration with: Hengstenberg and Hengstenberg

Mankind ... will not willingly
admit that its destiny can be
revealed by the breeding of flies
or the counting of chiasmata.

Cyril Dean Darlington
Royal Society Tercentenary
Lecture 1960

# 3-D Analysis of the Flight Trajectories of Flies (*Drosophila melanogaster*)

Keywords:

*Drosophila*, Tracking, Computer reconstruction, Saccades, Free flight

Abstract:

A computer system for reconstructing and analyzing three-dimensional flight trajectories of flies and its application to the study of the free flight behaviour of the fruitfly *Drosophila melanogaster* is described. The main results are:

a) *Drosophila* males only occasionally track other flies;
b) in such cases the fly's angular velocity is a function of the error angle under which the leading fly is seen;
c) body saccades can be demonstrated during cruising flights;
d) high angular velocities are strongly correlated with low forward velocities, probably reflecting an aerodynamic constraint of flight.

The 3-D technique described may provide an adequate tool for studying the organization of the flight control systems present in flies and for relating the free flight behaviour to previous analyses of tethered flight.

## INTRODUCTION

Visual control of flight in flies has been approached in recent years by studying either the behaviour of tethered flies (Reichardt, 1973; Reichardt and Poggio, 1976, 1980; Wehrhahn and Reichardt, 1975; Götz, 1968, 1975; Götz et al., 1979) or the trajectories of freely flying flies (Land and Collett, 1974; Collett and Land, 1975, 1978; Wehrhahn, 1979). Until now neither approach has encompassed all dynamical degrees of freedom enjoyed by a freely flying fly. The analysis of free flight episodes mostly has been carried out by filming only projections onto one plane of three-dimensional trajectories. Although houseflies have been filmed simultaneously from above and from the side, lack of synchronization between the two cameras forbade a precise 3-D reconstruction (Wehrhahn, 1979). In order to overcome these limitations a computer-based system was developed (in cooperation with T. Poggio and C. Koch) to reconstruct and analyze the trajectories of freely flying flies in three dimensions. This technique and its use in a preliminary analysis of the 3-D trajectories of Drosophila melanogaster are described.

## MATERIAL AND METHODS

Flies were placed in a rectangular glass case (58 x 28 x 28 cm) homogeneously illuminated from two sides by dc-driven fluorescent light bulbs (1000 $cd/m^2$). The flies were filmed with a high-speed camera (Redlake Locam, model 51-0002) simultaneously from one side (x-z plane) and from above (x-y plane) through a mirror leaning forward at 45°over the box. The data presented here were obtained with a frame rate of 100 frames/s and an exposure time of 3 ms; the 16 mm film used was Kodak (Eastman Ektachrome Video News Film 7240 Tungsten, 125 ASA). The films were projected frame by frame on a digitizing tablet (Summagraphics-ID) with a single-frame projector (L-W International, Model 224; or Vanguard Motion Analyzer M-16C). For each frame the xy- and the xz-coordinates of each fly were digitized, together with a pair of fixed reference points, used by the computer (PDP-11/34) to correct possible errors of frame positioning. After perspective corrections, the "true" xyz-coordinates of each fly in each frame or even between frames (as given by a spline interpolation routine) were available for further processing by other programs. It is, for instance, possible to obtain stereoplots of the fly trajectories (Fig. 1) and to perform translation and rotation in 3-D space. The time history of several parameters characterizing flight - for example angular velocity, forward velocity etc. - can also be plotted,

together with their histograms, scatter diagrams (see Land and Collett, 1974), crosscorrelation and autocorrelation functions. In this way, relationships between visual input variables (such as the instantaneous error angle at which a fly sees a target) and output variables (such as the angular velocity of the tracking fly) may be discerned and analyzed. Since in the present analysis the fly is considered as a point in 3-D space, only 3 of the 6 degrees of freedom needed for a complete description of the body movement are taken into account. Neither the body posture nor the head position are directly determined in the present analysis. Accordingly, the error angles between the fly's direction of flight and the target in the horizontal ($\psi$) and vertical ($v$) direction, respectively, do not coincide with the angular position of the target's image on the fly's eye, whenever (1) the fly is moving obliquely to its long axis (Land and Collett, 1974), or (2) the head is deflected from its normal orientations to the body. Because of these limitations the present analysis of the control systems involved in a 3-D control of flight should be considered as a first-order approximation. The simulation of the trajectory of a chasing fly according to a 3-D version of a model of visual orientation behaviour in flies (Reichardt and Poggio, 1976, 1980) is achieved by an appropriate computer program.

## RESULTS

### a) Do *Drosophila* chase?

Land and Collett (1974) were able to film chases in which male flies (*Fannia canicularis*) pursue other flies. This kind of control system underlying this behaviour in *Fannia* and *Musca* has been described in some detail (Land and Collett, 1974; see also Reichardt and Poggio, 1976, 1980). It has been recently shown that female houseflies, tracking moving objects under artificial laboratory conditions (Virsik and Reichardt, 1974), can also track other flies in free flight (Wehrhahn, 1979). Tethered flying *Drosophila melanogaster* under artificial laboratory conditions show tracking behaviour similar in some respects to *Musca* (Zimmermann, 1973; Reichardt and Poggio, 1976). Although freely walking *Drosophila* males follow female flies during courtship, and females track other females under certain conditions (Bastock and Manning, 1955; Cook, 1979, 1980), no analogous behaviour in flight has been yet described. Whilst chasing episodes can be readily observed amongst captive male houseflies, in *Drosophila* the situation is less clear. Careful observation of about 15 minutes (98684 frames) of film has confirmed this impression. Not a single chasing episode could be observed comparable in accuracy and rapid changes of course with chases observed in male houseflies (Wehrhahn, 1979). In several instances, however, a fly was

apparently able to follow for short periods of time (maximum 500 ms) the course of another fly. One such short episode of "tracking" is shown in Fig. 1a. The almost straight path of the leading fly is a common characteristic of these flight interactions; sharp turns of the leading fly (as in Fig. 1b, c) were never followed by the other fly. For comparison with the flight behaviour of larger flies see in Fig. 6 the aerobatic chase between houseflies (digitized from a film kindly provided by C. Wehrhahn). From closed-loop tracking experiments with both Drosophila and Musca, it is known that a fly controls the torque around its vertical axis as a function of the horizontal error angle $\psi$. The $\psi$ we have measured does not necessarily represent the horizontal position of the target on the fly's eye (as in closed-loop experiments), because of uncertainty about body direction and head position. It may be assumed, however, that it approximates the target's actual position (Land and Collett, 1974). Closed-loop experiments (Reichardt and Poggio, 1976) and free observations (Land and Collett, 1974) of houseflies suggest that the angular velocity $\dot{\alpha}$ in a horizontal plane is proportional, to a first approximation, to the torque around the vertical axis, since the inertia of the fly is negligible compared to its (aerodynamic) "friction" coefficient. Independent measurements on tethered flies free to rotate around the vertical axis have confirmed these estimates (Geiger

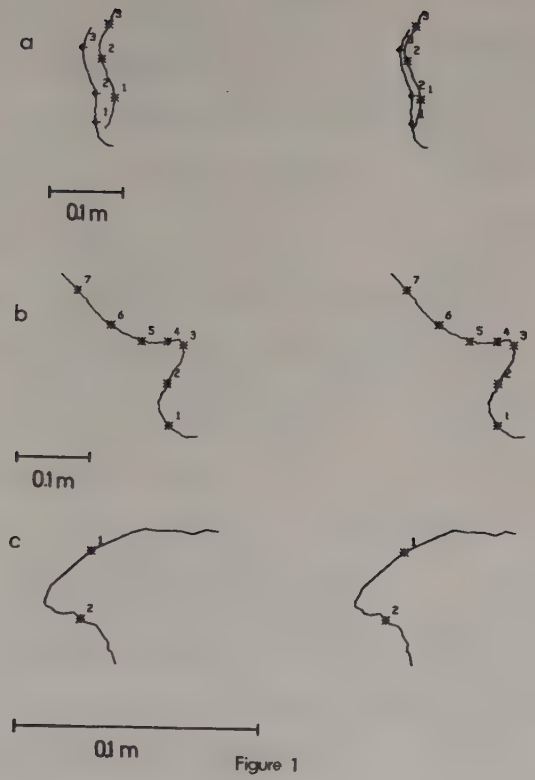



Figure 1

Stereo plots of 3-D flight trajectories shown in this figure should be observed with standard stereoglasses. (a) flight interactions in which a Drosophila male (◄) apparently tracks another male (*). Corresponding instants in the two flight paths are numbered at 100 ms intervals. (b) a cruising flight of a "single" Drosophila male in 3-D. Turns are almost never completely horizontal. They are often accompanied by significant vertical displacements. (c) another "idling" flight of a Drosophila male showing simultaneous turns in horizontal and vertical direction.

and Poggio, 1977). In Drosophila the surface-to-volume ratio is increased by a factor of about four. Accordingly, the inertia seems to be even more negligible. We therefore assume that acceleration components may be negligible also for the remaining degrees of freedom. For these reasons (and since our data are limited to 3 degrees of freedom) we will consider the angular velocity of the fly around its vertical axis as representative of its torque. As a consequence, we expect that the presence of a tracking system controlling the torque as a function of the error angle should be seen by a correlation between $\psi$ and $\dot{\alpha}$ with a certain delay $\epsilon$ (for Musca and Fannia males $\epsilon$ = 20-30 ms). The scatter diagram of Fig. 2 shows that for Drosophila there is indeed a significant relationship between $\psi$ and $\dot{\alpha}$. This relationship is roughly linear for $-50° < \psi < 50°$; the maximum of the cross-correlation between $\psi$ and $\dot{\alpha}$ indicates a delay in the order of 20-30 ms. These results suggest that the short interactions observed in free flying Drosophila may show a tracking behaviour similar to the one inferred from closed-loop experiments in Drosophila (Zimmermann, 1973; Heisenberg and Wolf, 1979) and from closed-loop and free flight data in houseflies.

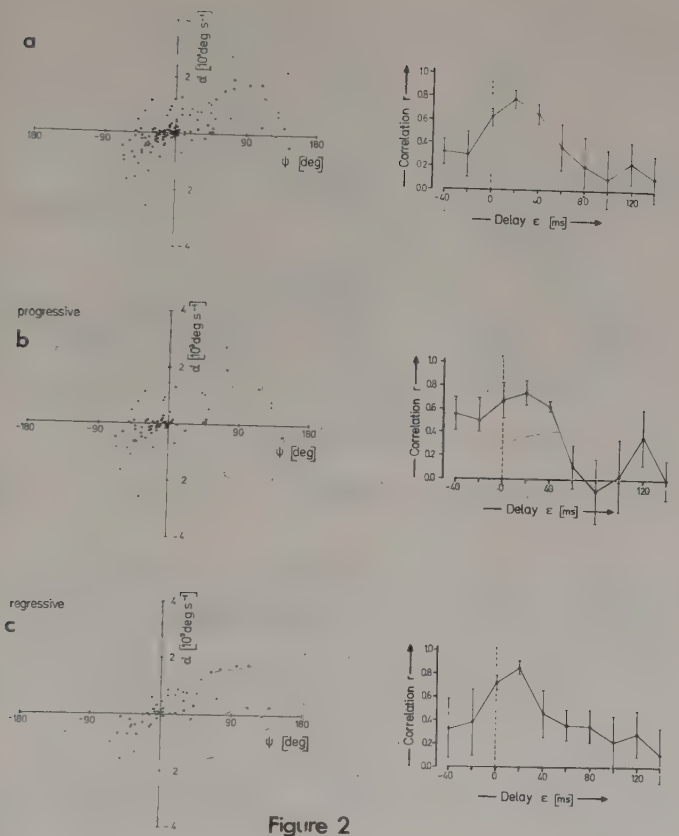



Figure 2

(a) Scatter diagram showing that the angular velocity of the following Drosophila males $\dot{\alpha}$ and therefore the torque arecontrolled by the horizontal error angle $\psi$. The diagrams on the right show the correlation coefficient and its standard error of the mean as a function of the delay. The maximum of the correlation between $\psi$ and $\dot{\alpha}$ occurs for a delay of between 20 and 30 ms. The scatter diagram is plotted for this delay. The slope of the regression is about 21 $s^{-1}$ (roughly the same value has been measured in tethered Musca, in free flying Fannia and in free flying Musca). The data are taken from 6 tracking episodes for a total of about 2500 ms flight.
(b) Scatter diagram of the data in (a) due to progressive (front-to-back) displacements of the target within the visual field.
(c) Same for displacements in the opposite direction.

Similar scatter diagrams show that Drosophila (either male or female) are probably unable to effectively control their forward velocity as a function of the distance from the target, similarly to female Musca and unlike male Musca (Wehrhahn, 1979). This result suggests that tracking episodes in Drosophila flights are a (necessary) byproduct of a fixation system, more concerned with fixation of objects to land on (Wehrhahn, 1979). The correlation between the vertical velocity $V_z$ (associated with the fly's lift) and the vertical error angle $v$ is rather poor in Drosophila. In Musca this degree of freedom is controlled almost as efficiently as rotation around the vertical axis (Wehrhahn and Poggio, in prep.). For male Drosophila most tracking episodes digitized so far (4 out of 5) show that the following fly is at, or below, the level of the leading fly (Fig. 3). Since the exact position of the head during flight is not known, $v$ does not exactly represent the vertical location of the target's image on the eye.

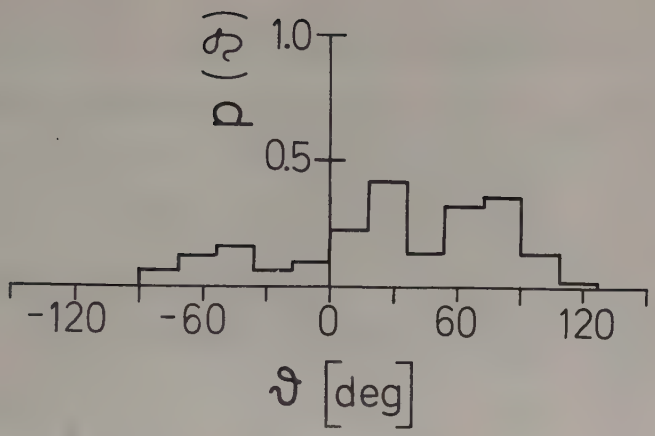



Figure 3

Frequency histogram of the vertical error angle $v$ of 5 chasing Drosophila males (Binwidth: 18 deg), showing that the males track other flies mostly from below (positive vertical error angle $v$). Only 1 out of 5 males was tracking from above.

The results obtained, so far, confirm the observation that courtship tracking is hardly initiated or maintained in flying pairs of Drosophila melanogaster. It is possible, however, that flight is important for courtship in other respects. Courtship stimulating pheromones may be perceived by males during flight, and these could determine gross course control (Bastock and Manning, 1955; Cook, 1979, 1980) and even a landing site.

b) An aerodynamic property of flight

As already observed in Fannia (Land and Collett, 1974), forward velocity (associated to the fly's thrust) is coupled to angular velocity. Scatter diagrams (Fig. 4a) reveal a maximum in the cross-correlation for 0 ms delay, for all flies (leading, chasing and idling), as expected in case of a purely aerodynamic phenomenon.

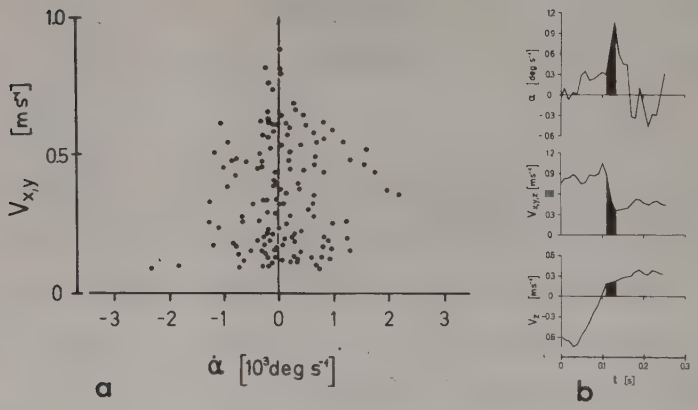



Figure 4

(a) Relationship between translatory (Vx,y) and rotatory ($\dot{\alpha}$) velocity in the xy-plane for 6 different flies. Maximum correlation always occurs for 0 ms delay. The scatter diagrams are essentially the same for idling, leading or tracking flies, respectively.
(b) Time course of the rotatory velocity $\dot{\alpha}$ , and of the translatory velocities in forward (Vx,y,z)and upward (Vz) directions for the saccade shown in Fig. 1c. The forward velocity is decreasing monotonically during the accelerating phase of the saccade. The lower plot shows that the fly is climbing with an almost constant rate during the saccadic maneuver.

The data can be interpreted in the following way: there is an upper limit to the 2-D forward velocity and this limit decreases monotonically with angular velocity (from about 1.0 m $s^{-1}$ at $\dot{\alpha}$ = 0 deg $s^{-1}$ to approximately 0.3 m $s^{-1}$ at about $\dot{\alpha}$ = 2000 deg $s^{-1}$; see Fig. 4a). Interestingly the observed maximum angular velocities exceed the values expected from the torque measured in tethered flies. From closed-loop experiments an estimate of the relation between torque and angular velocity leads to an upper limit of 87 deg $s^{-1}$ per $10^{-9}$ Nm (Zimmermann, 1973; Heisenberg and Wolf, 1979). Published peak values of Drosophila torque are below 4 · $10^{-9}$ Nm (Zimmermann, 1973; Heisenberg and Wolf, 1979) corresponding therefore to peak angular velocities of less than 400 deg $s^{-1}$. Significantly higher angular velocities seem possible in free flight (2000 deg $s^{-1}$ in Fig. 2a and 4000 deg $s^{-1}$ in the inset of Fig. 5a). This result cannot completely be attributed to the sampling error of the digitized data which impairs the accuracy of the determination of the angular derivatives of the trajectory. There must be additional mechanisms in free flight which increase the effective torque produced by the fly. Firstly the torque may be effectively increased by aerodynamic effects of the streaming air (Vogel, 1966). Moreover, steering by posture of the legs and the abdomen (Götz, et al., 1979) and one sided breaking by posture of

the wing on the inner side of the curve (Nachtigall and Wilson, 1967; Magnan, 1934) may produce, in free flight, torque components which do not occur under tethered conditions in still air. The torque component associated with braking would be generated mainly at the expenses of forward thrust. This is consistent with the relation between $V_{x,y}$ and $\dot{\alpha}$ in Fig. 4. Steering by posture of the legs and of the abdomen has been shown to be under visual control (Götz et al., 1979). The torque component possibly provided by braking during free flight may be controlled by the visual input according to rules somewhat different from the ones obeyed by the torque component measured in tethered flying flies. The delay may be shorter and position information may not depend on directional movement.

c) Evidence for body saccades

It has been recently proposed that the tethered Drosophila performs body torque saccades around their vertical axis (Heisenberg and Wolf, 1979). The standard criterion for the definition of saccades, as used for vertebrate eye movements, relies on their comparatively fast time course (Reichardt and Poggio, 1980; Collett and Land, 1975, 1978; Geiger and Poggio, 1977). According to this criterion the presence of body saccades in free flight could be revealed by a multimodality of the histograms of $\dot{\alpha}$ , indicating the existence of "normal"

as well as saccadic processes with different time course. While histograms of $\dot{\alpha}$ during tracking interactions are unimodal for both flies (Fig. 5a), the situation is different for some " idling " (non tracking) flights selected for their sharp turns. Fig. 5a shows that in this case $\dot{\alpha}$ has a trimodal distribution, strongly suggesting the presence of a fast process of arbitrary sign in addition to the slow, roughly gaussian, stochastic torque process described by Reichardt and Poggio, 1976. The saccadic nature of the associated turns can be seen from the time course of $\dot{\alpha}$ (inset of Fig. 5a) and can be compared with the saccades observed in Syritta (Collett and Land, 1975, 1978) and the "torque spikes" found in Drosophila (Heisenberg and Wolf, 1979). The duration of the saccades varies between 50 ms and 100 ms and their peak velocities between 2000 deg $s^{-1}$ and 5000 deg $s^{-1}$. Each of the four observed saccades leads to a total angular shift of about 100 deg. In this respect, they are different from the much smaller and longer torque spikes measured in a tethered Drosophila but similar to the body saccades generated if the tethered fly is free to rotate around its vertical axis (Heisenberg and Wolf, 1979).

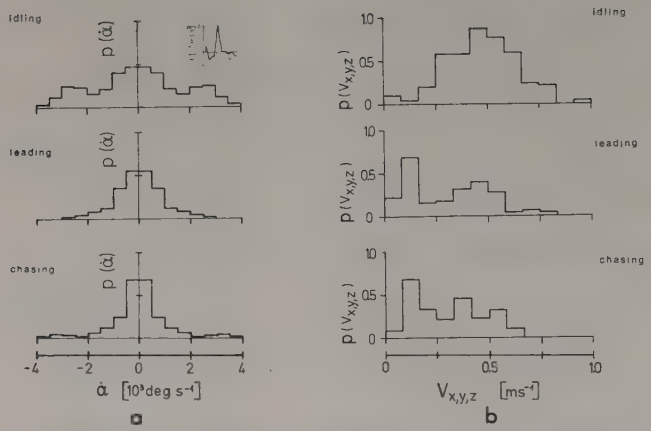



Figure 5

(a) Frequency histograms of the rotatory velocity ($\dot{\alpha}$) in the xy-plane for "idling" (upper plot), "leading" (middle plot) and "chasing" (lower plot) Drosophila (Binwidth: 500 deg $s^{-1}$). In the first case the histogram is consistent with the presence of two processes of different time course, a slow (continuous) process and a fast (saccadic) process of arbitrary sign. The "idling" fly data are taken from 4 flight episodes (or a total of 1700 ms), each showing one saccade-like turn. The time course of such a turn is shown in the inset. The diagrams below refer to 5 tracking episodes, or about 2100 ms of flight.
(b) Frequency histograms of the translatory velocity (Vx,y,z) in space for "idling" (upper plot) "leading" (middle plot) and "chasing" (lower plot) Drosophila (Binwidth: 0.1 m $s^{-1}$). The data are taken from the same flies as in Fig. 5a.

The apparent absence of saccades during tracking reflects the fact that the fixation system is, most of the time, in a nonsaccadic, continuous mode. A saccade of the leading fly is likely to disrupt tracking. The free flight data rule out the possibility that these sharp turns in the xy-projection of the trajectory are an artefact of the 3-D nature of the flights. The additional analysis of 3-D angular velocity supports these conclusions and indicates the presence of a fast process for "idling" rather than chasing. Another possible difference between idling and chasing flies can be seen in the histograms of the 3-D forward velocities (Fig. 5b).

## CONCLUSIONS

The technique introduced here facilitates the analysis of the control systems used by flies for visual guidance during flight, including tracking, fixation and landing. A more complete 3-D description of the input-output relations involved in visually guided behaviour becomes feasible with further development of the computer program. Using this technique it will be possible to compare the behaviour of flies in free flight to that displayed by tethered flies. This may be relevant for the interpretation of electrophysiological data obtained from the movement detecting centers of Musca. It has been proposed repeatedly (Reichardt, 1973; Götz, 1972; Götz and Wenking, 1973; Zimmermann, 1973; Wehrhahn and Hausen, in press) that the conversion of the angular error into torque towards the target may result from the motion of the target's image on the eye of the flies. During tethered flight, motion progressing from front to back is actually eliciting stronger reactions than motion regressing from back to front. However, the comparison of the scatter diagrams (Fig. 2b, c) do not show significant differences of the responses to progressive (slope and S.E.M.: $17 \pm 4\ s^{-1}$) or regressive ($23 \pm 4 s^{-1}$) motion. The underlying question whether or not the behaviour in free flight is sufficiently predictable from the responses obtained during stationary flight has

been addressed in the analysis of similar 3-D data for Musca. Fig. 6b shows a 3-D simulation of the flight shown in Fig. 6a which has been calculated in cooperation with T. Poggio and C. Koch. Inserting the parameters obtained during stationary flight in the corresponding model applied in this simulation (Poggio and Reichardt, 1973, Reichardt and Poggio, 1976, 1980) produces the trajectory of the chasing fly from the trajectory of the leading fly. Comparison with the actual tracks shows that the present model is obviously sufficient to produce some features of 3-D-tracking in remarkable detail. The addition of a "looking around" or "noise" term (Reichardt and Poggio, 1976) to the phenomenological equations of the model does not change significantly the simulated trajectories. Moreover, the simulation in Fig. 6b involving either a linear $\psi$ -torque transduction (Land and Collett, 1974; Reichardt and Poggio, 1980), and the simulation in Fig. 6c involving a position-dependent reaction restricted to progressive stimulus motion (Wehrhahn and Hausen, 1980), are both roughly equally successful. Actually, the associated differential equations are indeed isomorphic if compared on a "coarse" time scale (Poggio and Reichardt, unp.).

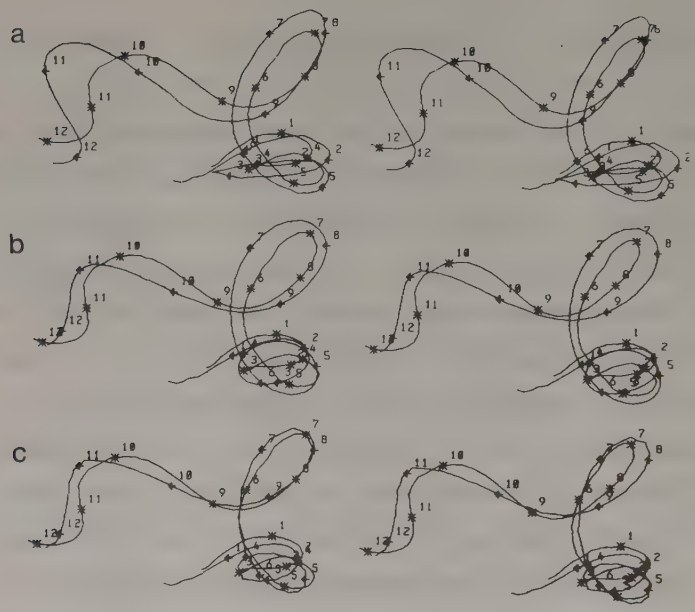



Figure 6

(a) Stereo plot of a 3-D chase between flies Musca domestica.
(b) Simulation of the same chase according to an algorithm based on the phenomenological theory of pattern orientation by Reichardt and Poggio: The algorithm computes from the xyz-coordinates of the leading fly (*) and of the chasing fly (◄) the expected torque, lift, and thrust of the chasing fly, translates these coordinates into angular velocity, upward velocity and forward velocity from which the 3-D trajectories are derived.
(c) Another simulation of the trajectory in which the contribution of regressive target motion has been neglected. Redrawn from Poggio and Reichardt (1981).

In summary, the 3-D analysis of flight trajectories shows that Drosophila melanogaster males are able to track other flies. These tracking episodes are, however, comparatively rare and short. Saccadic changes in angular velocity (Heisenberg and Wolf, 1979) which have been clearly identified in the records of free flight cruising seem to be missing during the free flight tracking maneuvers of the males.

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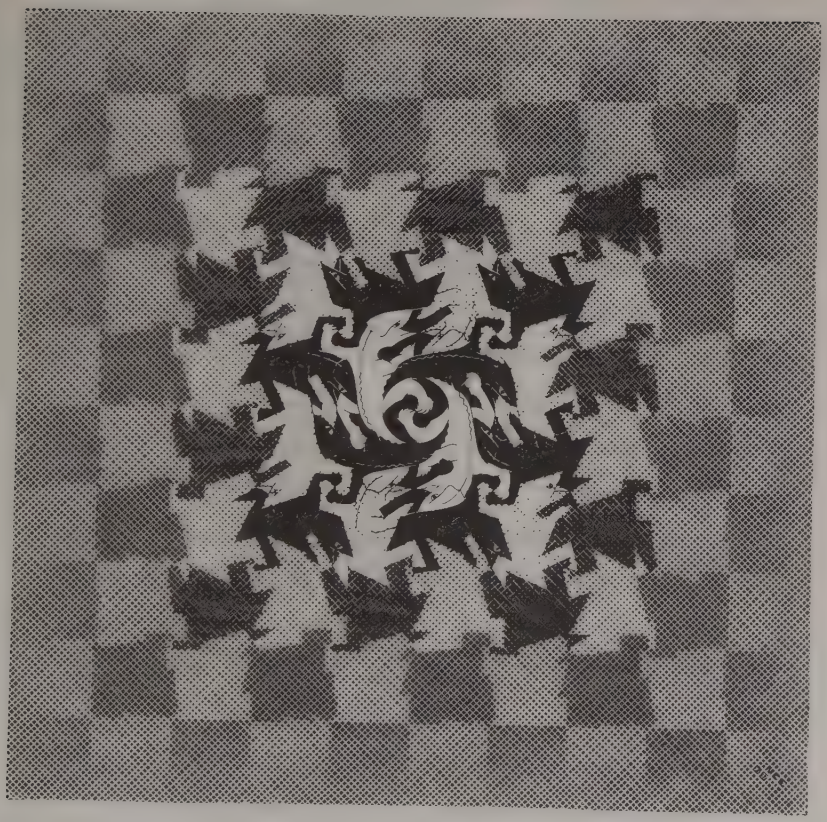
# PART 2

## Figure-Ground



M. C. ESCHER

# Figure-Ground Discrimination in the Visual System of *Drosophila melanogaster*

Keywords:
*Drosophila*, Visual Guidance, Figure-Ground Discrimination, Open Loop and Closed Loop Behaviour

Abstract:
*Drosophila melanogaster* is able to detect a small visual object hidden in an equally textured background as long as there is a relative motion between their retinal images. The principle of figure-ground discrimination in the walking fly are studied under experimental conditions where the positions of figure and ground are oscillating sinusoidally with similar frequency and amplitude but with different phase. The following has been established.

a) the turning reaction of the stationarily walking *Drosophila* depends on the phase; contrary to the results obtained with the flying *Musca* (Reichardt and Poggio, 1979), antiphasic oscillation of figure and ground does not exclude the detection of the figure.

b) a translatory response has been found which also depends on the phase difference of the oscillatory movements of figure and ground.

c) the time course of the responses and its intra- and interindividual variability do not seem to fit into a rigid model of figure-ground discrimination.

## INTRODUCTION

Camouflage is a nice trick developed by nature to hide a motionless prey in the environmental background. To detect, for example, a motionless moth in a tree requires very complex pattern recognition capabilities. Even for a human observer it is difficult to find a small object embedded in a randomly textured background. However, the hidden object becomes suddenly visible when it starts to move relative to this background. Even a figure consisting of the same random texture as the background is clearly visible as a coherent entity as long as it is moving. When the figure is not moving against the background its boundaries disappear in the random texture of the ground and the detection may become almost impossible. With the instructions given in the legend of Fig. 1 it is easy to produce this striking phenomenon.

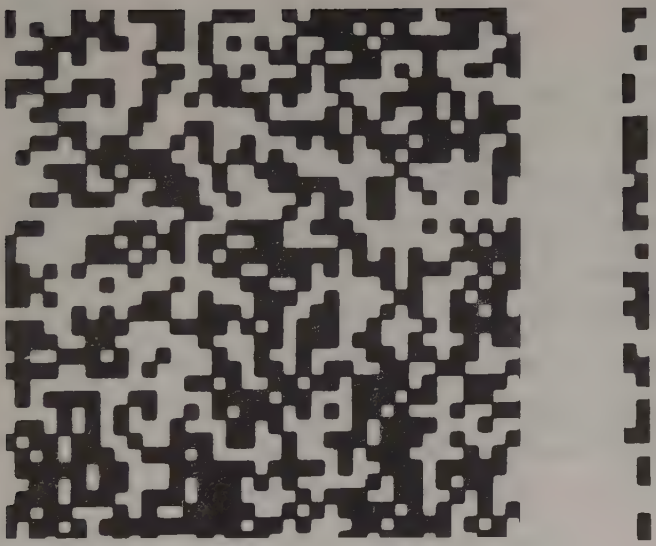


Figure 1

To demonstrate the figure-ground separation effect it is suggested to cut out the small randomly textured stripe, the "figure", and to move it against the random "background" pattern of the same texture. As long as there is a relative motion between figure and ground the boundary of the figure is clearly visible and the figure is perceived as an entity. However, when figure and ground are not moving relative to each other the boundary of the figure disappears in the texture of the background. Due to the poor resolving power of the fly's eye the random pattern used in the fly experiments is comparatively coarse.

The first demonstration of this effect in insects was given by Virsik and Reichardt (1974, 1976) in a series of closed-loop experiments in which a fixed flying Musca could track a small object in front of a random background as long as there was a relative motion between figure and ground. Fig. 2 shows that the walking fruitfly, Drosophila melanogaster, also behaves the same way when it is confronted with a similar situation. Flies frequently try to approach visually distinct objects on a bright background (for a review of the "fixation response" see Reichardt and Poggio, 1976; Poggio and Reichardt, 1976). As shown in Fig. 2 relative motion of a small random figure in front of a similarly textured background also induces this fixation response in Drosophila: the figure vanishes, and the response disappears, when figure and ground are moving coherently. The present paper deals with the problem how Drosophila is separating figure from ground.

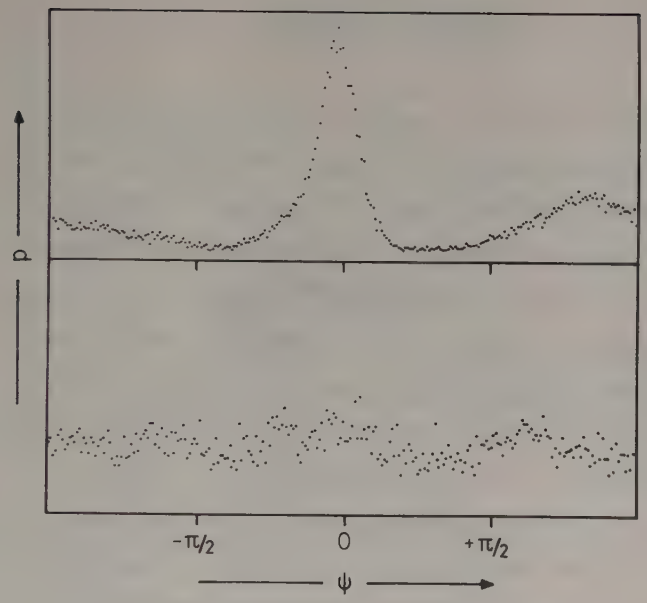



Figure 2

Closed-loop figure-ground experiment demonstrating that a stationarily walking Drosophila actually perceives a random pattern in front of a background of the same random texture. The data refer to 2 h of continuous registration of the locomotor activity of a fly in the experimental set-up is shown in Fig. 3. The diagrams represent the probability to find the figure in a given angular distance $\psi$ from the position in front of the fly ($\psi = 0$). The upper histogram shows that the intended turns of the fly are shifting the foreground stripe for most of the time in the frontal part of the visual field as long as the background pattern is at rest. If this background pattern is locked to the closed-loop movements of the foreground stripe the fly does not seem to be able to fixate the stripe (lower histogram).

## MATERIAL AND METHODS

Evaluation of experiments such as in Fig. 2 requires the analysis of a large amount of behavioural data. The automatic registration of the optomotor responses shown in Fig. 3 is adopted from Buchner's test apparatus (Buchner, 1976) and is described in detail in another paper (Bülthoff, 1981a). It is based on a dotted ball of 1 cm ø floating on air on which a fixed fly could easily walk by turning the ball in any direction. The movements of the dots are resolved by a 4-quadrant photodiode in a small area behind the fly and near the equator of the ball. A sequence detecting electronic device is triggered when the black dots on the ball sequentially darken the different segments of the photodiode. The horizontal and vertical components of the movement of dots across the photosensitive device correspond, respectively, to the rotatory and translatory movements of the fly. The achievment of the present design is the comparatively high resolution of about 9° for rotation displacements and about 0.08 cm for translatory displacements of the ball. Continuous representation of the intended rotatory responses of the tethered fly is a prerequisite of a successful control of the angular position of the visual environment by the responses of a test fly in a closed-loop experiment, such as Fig. 2.

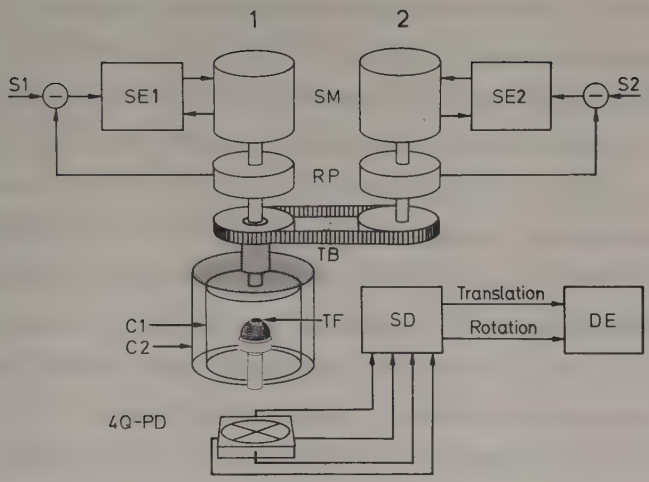



Figure 3

Schematic representation of the experimental set-up used in figure-ground experiments. A fixed test-fly (TF) is walking on a small styrofoam sphere floating on air. A 4-quadrant photodiode (4-Q P D) and a sequence detecting logic (SD) resolve the movements of the dots on the ball into horizontal and vertical components which correspond, respectively, to the rotatory and translatory movements of the fly. For on-line data evaluation (DE) a signal averager was used. The fly is surrounded by two transparent cylinders (C1 and C2) to which the foreground (not transparent) and background patterns can be attached. C1 is driven directly by servomotor SM1, C2 is driven via a transmission belt TB by SM2. The movements of the cylinders are controlled by the ringpotentiometers RP whose outputs are fed back to the servomotor electronics SE1 and SE2. Thus, the servomotors are driven under position control. The angular displacement of the cylinders are therefore strictly proportional to the input signals S1 and S2 of the servo electronic.

Independent control of the angular position of figure and ground is obtained by two concentric transparent cylinders which are driven by independent servomotors under conditions of position control. The texture of the patterns inside the cylinders consists of a computer-generated random array of black and white rectangles of 15 x 15° as seen by the fly. To maintain the apparent size for latitudes up to ± 45° within the visual field, the rectangles had to be extended in height to compensate the effects of inclination and distance (Götz,1964). The comparatively coarse texture of the patterns was chosen to avoid geometric interference effects between the pattern and the regular array of visual elements in the fly. The characteristic spatial wavelength of the texture elements is well above the critical value of twice the sampling base of the movement detectors for horizontal displacements (Buchner, 1976). The figure pattern is a vertical stripe, two picture elements wide and indistinguishable from the background texture. In the open-loop figure-ground experiments described below the figure is moving slowly around the fly (10°/s) in alternating clockwise (cw) and counterclockwise (ccw) directions, while figure as well as ground are oscillating sinusoidally with the same frequency and in a given phase relation. In some experiments the background was also drifting in alternating directions but with much lower velocity (0.7°/s) than the foreground. This is to obtain a comparatively homogeneous distribution of

possible stimulus conditions over the different angular positions within the visual field of the fly. For each of the flies the rotatory and translatory walking responses were averaged, as a function of the angular foreground position, by an on-line computer (Histomat S, Deutsche Intertechnique, Mainz, W.-Germany). The phase relation between figure and ground oscillation was changed systematically after five cycles of the slow cw/ccw rotation of the foreground. The comparatively long lasting open-loop experiments with a stationarily walking fly allows to determine the"attractiveness" profile of the figure, over up to 12 successive time periods of 12 - 18 h, for different phase relations and different oscillation frequencies. This allows the comparison of phase, frequency and time dependence of the figure-ground discrimination process for the rotatory and translatory component of locomotion of the same fly. Most of the experiments described below are performed with 3 - 8 days old female wild type Drosophila melanogaster from the inbred laboratory strain "Berlin" or a local strain (Kapelle). Drosophila males were used in a few experiments only.

## THEORETICAL BACKGROUND

The computational problem of detecting an object embedded in a "noisy" background by its relative motion is to detect discontinuities in the velocity field, because discontinuity implies, under the tacit assumption of object rigidity, the presence of at least two different objects. It can be shown (Poggio and Reichardt, 1976, 1980; Reichardt and Poggio, 1979, 1980) that the signals of at least 4 separate inputs have to interact non-linearly in order to detect these discontinuities. A more detailed theoretical analysis is in progress (Bülthoff et al., 1980). The conjecture according to which elementary movement detector outputs have to be compared can be understood intuitively. Since discontinuities in the field of velocities are considered it is clear that the output of elementary movement detectors aiming at different areas of the environment must be compared. This procedure could take a number of different forms. For simplicity two comparatively simple alternative algorithms implementing relative movement detection are discussed in the following.

In the first case the interacting elementary movement detectors are of the direction-sensitive (ds) type. Computer simulations of the responses of an array of ds-movement detectors in a figure-ground

situation have shown that the detection of an object can be reduced to the detection of discontinuities in the sign of the detector outputs. If there is a phase difference $\varphi \neq 0$ between the oscillatory movements of figure and ground then it is obvious that the sign of any two ds-detector signals for figure and ground, respectively, must be different during a fraction $0 < \tau < 1$ of each time period of the oscillation. The minimum $\tau = 0$ refers to zero phase difference ($\varphi = 0$). The maximum $\tau = 1$ is expected during antiphasic oscillation of figure and ground ($\varphi = \pm 180°$). If any two ds-movement detectors interact by multiplication of their respective output then the phase dependence of the average response at a given oscillation frequency ($\omega$) can be approximated by

$$\bar{R}_{ds}(\varphi) \propto K_0(\omega) + K_1(\omega) \cos \varphi .$$

The situation is different in the second case where the interacting detectors are of the direction-insensitive (di) type. In this case the detector outputs equal each other for $\varphi = 0$ as well as $\varphi = +180°$. The difference between the movements of figure and ground is only in the direction of movement to which these detectors are insensitive. The phase dependence of the average response should therefore show a minimum at 0° and 180°. A maximum is expected for phase differences of $\varphi = 90°$ and $\varphi = 270°$, respectively, where maximum velocity in one of the detectors and zero velocity in the other is likely

to coincide. The corresponding phase profile is well approximated by

$$R_{di}(\varphi) \propto K_0'(\omega) + K_2'(\omega) \cos 2\varphi .$$

Any combination of these two different models of figure-ground discrimination is of course feasible.

## EXPERIMENTAL RESULTS

The attempt to determine the algorithm used by the fly to detect relative movement, or to discriminate figure and ground, requires experiments on the phase dependence of "attractiveness". In Fig. 4 the rotatory and translatory attractiveness profiles of a fixed walking Drosophila melanogaster are shown for an 8-hour-experiment during which the phase relation between 1.5 cps oscillations of figure and ground was changed every 12 minutes in steps of 45°. Every 1.5 hours a cycle of 0° to 360° phase difference was completed and started again. Drosophila is clearly able to detect the figure against the background whenever there is relative movement. Very interestingly, also the translatory component of the walking reaction of Drosophila is sensitive to relative movement and to the phase between the oscillations of figure and ground. From the 3-dimensional representation in Fig. 4 it is easy to recognize the characteristics of the phase dependence of the rotatory and translatory responses, respectively. The collected results shown in (a) are redistributed in (b) according to the actual phase difference of the oscillation of figure and ground. The profiles obtained illustrate both the effect of a particular phase and the time course of this effect in intervals of 1.5 h duration. The diagrams show the influence of fatigue, habituation or other internal states of the fly on the response at a given phase.

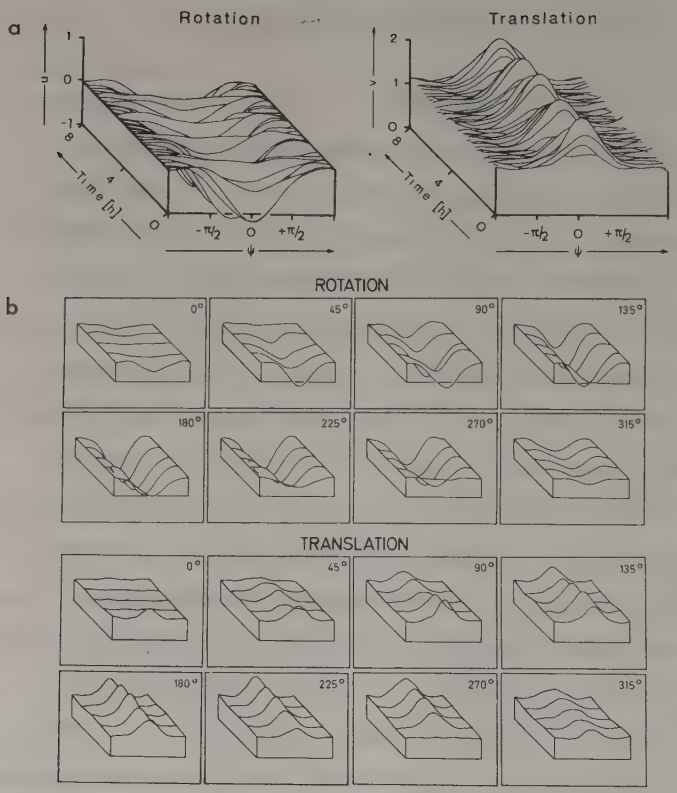



Figure 4

(a) Rotatory and translatory optomotor response registered over 8 hours in an open-loop figure-ground situation described in the text. The 3-dimensional representation of the data demonstrates a strong dependence of "attractiveness" on the phase between the oscillations of figure and ground. The phase relation changes every 12 minutes in steps of 45°. The rotatory response refers to the potential given by the running integral of the attractiveness profile. The translatory response denotes the forward velocity with respect to the position $\psi$ of the figure within the visual field of the fly.
(b) The different phase relations of (a) are plotted separately to elucidate the phase and time dependence of the figure-ground discrimination process in Drosophila.

The temporal increase in the rotatory and translatory effects obtained, for instance, with antiphasic oscillation ( $\varphi = \pm 180°$), and the concomitant temporal decrease in the effects obtained at two other phase angles ( $\varphi = 45°$, $\varphi = 90°$) demonstrates a remarkable nonstationarity of the figure-ground response which is either a specific feature of Drosophila or a more common trait of fly behaviour likely to be found in corresponding experiments of similar duration. The results of Fig. 4 are summarized in Fig. 5. The diagrams in (a) show the time average, and the Fourier components, of the attractiveness of the figure in terms of the depth of the corresponding "potential" of the rotatory response. The abscissa denotes the phase between the oscillation of figure and ground. The diagrams in (b) refer to the mean forward velocity as a function of this phase. The Fourier analysis reveals the fundamental component as the domineering constituent of the rotatory and translatory response of Drosophila. The contribution of the second harmonic is comparatively unimportant. This favours a model of figure-ground discrimination comprising mainly movement detectors of the ds-type. The opposite result has been obtained with Musca under conditions of stationary flight. The predominance of the second harmonic in the behaviour of this fly is appropriately explained by a model comprising movement detectors of the di-type (Reichardt and Poggio, 1979).

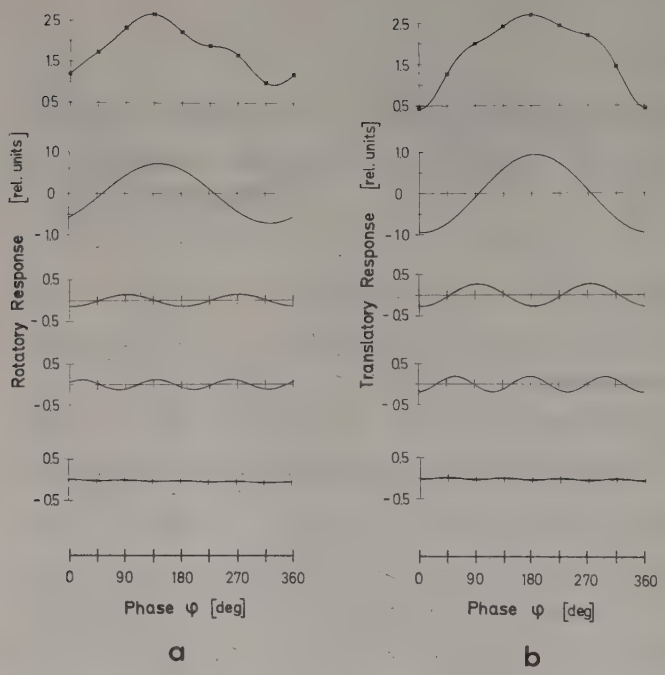



Figure 5

Phase dependence of the figure-ground separation effect. The uppermost diagrams show the average depth of the attractiveness potentials of the rotatory (a) and translatory (b) responses as a function of the phase differences between the oscillating figure and ground. For $0 < \varphi < 180°$ the figure is leading. The means of the data in Fig. 4 are fitted by the Fourier sum of the 4 harmonics shown in the lower diagrams. The separation effect is mainly due to the contribution of the first harmonic and is most conspicuous under the conditions of antiphasic stimulation ($\varphi = \pm 180°$). The response obtained at $\varphi = 0°$ is, most probably, a residuum due to the horizontal drift of $\pm 10° \; s^{-1}$ superimposed upon the horizontal oscillations of the figure in order to change its angular position $\psi$ with respect to the visual field of the fly.

The data presented, so far, refer to the response of only one fly. The intra- and interindividual variability in amplitude and phase of the first and second Fourier component found by analysis of the responses of 29 flies, obtained at oscillation frequencies between 0.5 and 5.0 cps, does not seem to fit into a rigid model of figure-ground discrimination. The rules accounting for preferences among the different strategies are far from being understood.

Evidently, the properties of the figure-ground response are intrinsic to walking Drosophila and not to the specific criterion, based on the measurement of "potentials". To prove this conjecture we elicited the figure-ground effect, in analogy to the experiments of Reichardt and Poggio on the flying Musca, by oscillating the stripe in front of the background at a fixed position on the right eye ( $\psi$ = 45°) and left eye ( $\psi$ = + 45°), respectively. The results are presented in Fig. 6. Again, the rotation response of Drosophila shows increased attraction for a phase shift of 180° between figure and ground which is missing in Musca.

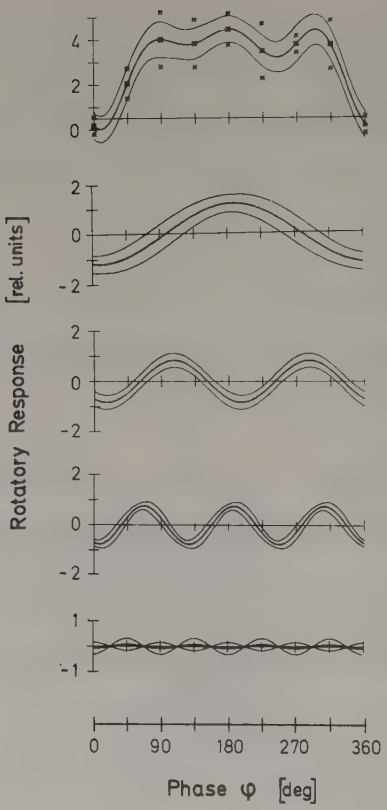



Figure 6

Phase dependence of the figure-ground separation effect under conditions where the figure is oscillating around fixed angular positions $\psi = \pm 45°$ on either side of the fly. The means and the standard errors of the means were fitted by the Fourier sum of the four harmonics shown in the lower diagrams. The data are given in relative units of "attractiveness", and refer to 120 h of continuous walk obtained with 5 flies. Permutation of the center position of the oscillating figure ($\psi$) and permutation of its phase difference with respect to the oscillating ground ($\varphi$) were initiated automatically every 120 s. Note the conspicuous separation effect obtained under the conditions of antiphasic stimulation ($\varphi = \pm 180°$). This effect is missing in the corresponding experiments with stationarily flying Musca.

Under the same conditions we also measured the actual time course of the response of Drosophila over 2 subsequent oscillation cycles of the ground. Each of the diagrams shown in Fig. 7 represents the average of about 9000 trials. Inspite of the comparatively high frequency (1.5 cps),and low amplitude (± 5°) of the input stimulus, there is still a remarkable modulation of the rotatory response. Drosophila is obviously able to resolve the oscillation and to follow the alternating direction of this movement stimulus. However, the signal-to-noise ratio of the phasic response is extremely low in these experiments.

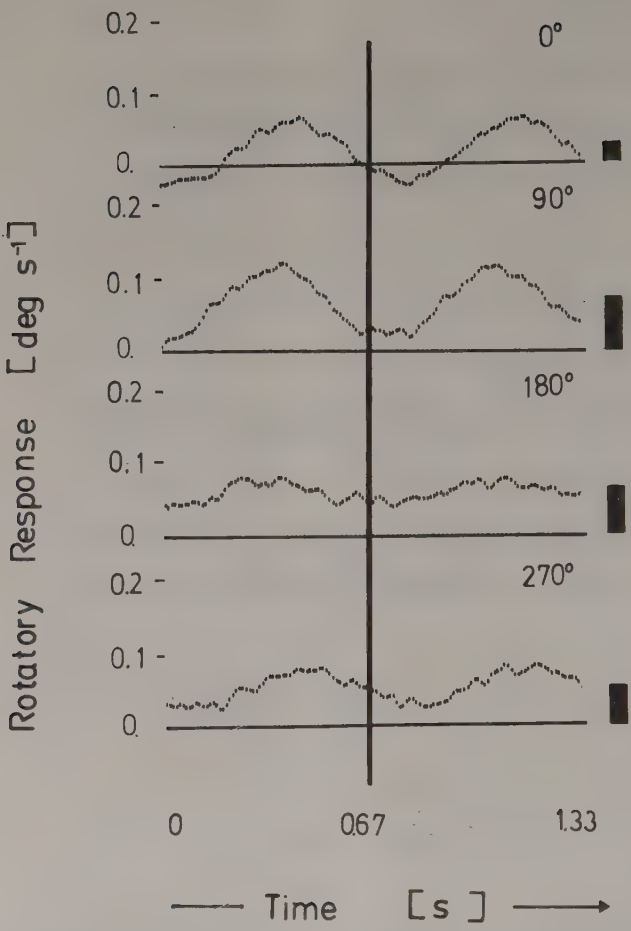



Figure 7

Phasic response of Drosophila to a small textured stripe oscillating in front of a textured background with an amplitude of ± 5° and an oscillation frequency of 1.5 cps. The curves represent the average rotatory response of 5 stationarily walking flies (same experiment as in Fig. 6) over 2 subsequent oscillation cycles triggered by the background at a mean stripe position of $\psi$ = 45° (right eye). The modulation of the response is significantly reduced for a phase shift between figure and ground of 180° and 270°. The bars in the right side of the diagrams denote the means of the response curves. The deviation from the mean response obtained with 0° phase shift is a measure of the mean attraction of the oscillating stripe as plotted in Fig. 6.

## DISCUSSION

The phasic response of *Drosophila* is different from the response of *Musca* which shows pronounced peaks at $\varphi = 90°$ and $\varphi = 270°$ phase difference between figure and ground (Reichardt et al., 1980). However, its general dependence on the phase difference (such as the decrease in modulation on the transition from $\varphi = 0°$ to $\varphi = 180°$) is consistent with the neuronal model recently proposed by Reichardt et al. (1980). In their scheme, elementary movement detectors are inhibited through shunting inhibition by large field cells responding to progressive and regressive motion in extended areas of the visual field. Shunting inhibition here implements an approximation to the multiplication-like interactions between movement detectors, required by the algorithms mentioned in the theoretical section (Bülthoff et al., 1980). The output of each of the elementary movement detectors is subject to a simple non-linear transformation at the level of the synaptic transduction, producing the square of the detector response. Integration of these responses is assumed to occur in the lobula plate. To account for the absence of the characteristic dynamics found in *Musca*, it appears sufficient to assume a linear transformation of the detector output at the level of synaptic transduction. However, the variability of the phase dependence of the figure-ground response in *Drosophila* requires further

amendments of the model. Its circuitry must in fact satisfy the constraint borne out by our experiments thatchanges in one of few components like synapse efficiency or weight of signals lead to a different dependency of the response on the phase.

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# PART 3

# Behavioural Genetics

PUIG ROSADO

# *Drosophila* Mutants with Specific Defects in the Visual Perception of Movement and Position

Keywords:
*Drosophila* mutants, Behavioural Genetics, Orientation, Movement, Position

Abstract:
A Y-maze paradigm for the selection of mutants of *Drosophila melanogaster* disturbed in visual orientation is described. Eleven probably new mutants have been isolated in this way; in addition, 24 already known mutants were tested. The following main results were obtained:

a) most of the isolated mutants show defects in the periphery of the visual system; 6 ERG mutants (2 probably new complementation groups) and 3 mutants with defects in the dioptric apparatus and the screening pigment;
b) only 2 strains are probably central nervous system (CNS) mutants, showing defects in the computation of both position and movement;
c) one mutant (*nofC*$^{B12}$) shows strong avoidance of small patterns moving with high velocity;
d) this inversion of the pattern-induced orientation response can be attributed mainly to a modification of the responses to progressive (front-to-back) movement.

In view of these results the possible decompositions of the overall optomotor behaviour in a set of genetically independent modules are discussed.

## INTRODUCTION

During the last decade a new field of behavioural genetics has been established with the aim to study the assembly and function of the nervous system. Production and assembly of the circuit components of behaviour (from the sensory input via the central nervous system to the motor output) are directed by the actions of genes. A mutation may disrupt the normal neural development and function of the nervous system and may alter the behaviour. The study of the components of behaviour is, therefore, facilitated by at least two genetic methods:

1) The mosaic technique is a micro-surgical tool to transform, on a statistical basis, specific parts of the nervous system into mutant genotype. The primary focus of a mutation can be easily localized by this method. By the use of temperature-sensitive mutants it is even possible to switch on and off the behavioural defect (Grigliatti et al., 1973), and thus to determine the ontogenetic schedule according to which the different effects of the mutation on the adult are initiated. Probing the mutants with electrophysiological techniques has given essential insights especially into the neuromuscular system of Drosophila (Ikeda and Kaplan, 1970; Alawi and Pak, 1971; Levine and Wyman, 1973; Ikeda et al., 1976; Siddiqui and Benzer, 1976; Heide, 1978; Ewing, 1979).

2) The second method widely in use is the selection technique for single gene changes which lead to abnormal behaviour. By this technique the normal behaviour can be dissected into its components. Drosophila was chosen as the experimental animal by different groups because of its well established genetics. The first step in this approach is the isolation of a relevant mutation in the offspring of mutagenized flies. One has to find a simple method for testing thousands of flies for a specifically abnormal behaviour. The more specific the abnormal behaviour is, the more specific the test has to be in order to suppress the selection of unspecific mutants. If one is interested, for example, in the phototransduction processes, it is more convenient to screen for phototaxis mutants than to look with electrophysiological methods directly at the photoreceptors of single flies. Since Benzer(1967) has isolated phototaxis mutants according to the sign and strength of their fast phototaxis response as well as to their locomotor activity, many different phototaxis mutants have been found by different groups (Pak and Pinto, 1976; Hall and Greenspan, 1979).

Visually guided movement of insects involves highly specific processing of visual information and is, therefore, an attractive paradigm for the dissection of a nervous system in Drosophila. The movement-induced course control (optomotor response) stabilizes the locomotion of the flying or walking fruitfly by correcting the course in the

direction of the visually perceived movement (Götz, 1968, 1973, 1975). By the pattern-induced orientation response (fixation response) flies such as Musca and Drosophila can localize and approach prominent objects (Reichardt, 1973; Reichardt and Poggio, 1976; Pick, 1976; Wehrhahn and Hausen, 1980; Zimmermann, 1973; Heisenberg and Wolf, 1979). They are able to track moving targets, even in front of a noisy background (Virsik and Reichardt, 1974, 1976; Reichardt and Poggio, 1980; Bülthoff, 1980b),and to chase other flies in flight (Land and Collett, 1974; Collett and Land, 1975; Wehrhahn, 1979; Bülthoff et al., 1980) and on the ground (Bastock and Manning, 1955; Cook, 1979, 1980). The starting, landing and escape reflexes are also under visual control. In recent years significant progress has been made in the understanding of the optomotor system of insects at different levels - the component, algorithmic and computational levels - (Marr and Poggio, 1977). The main tasks which have to be performed by the visual system of the fly are the computation of the position and movement of an object. For the computation of the position of a small object in front of a uniform background 1-input nonlinear flicker detectors are formally sufficient. At the computational level the detection of movement can be formally reduced to simple nonlinear multiplication-like interactions between adjacent pairs or groups of photoreceptors (Poggio and Reichardt, 1973a). For the more complex task of detecting a moving object in front of a

non-uniform background a minimum of 4-input nonlinear interactions is necessary (Poggio and Reichardt, 1980). Up to now it is not clear whether this distinction can be made also at the component (cellular) level. The independence of the different levels of understanding the nervous system can be demonstrated, for example, by the sexual dimorphism (Hausen and Strausfeld, 1980) in the orientation behaviour. The algorithm used to control the angular velocity is the same in tracking males and females. The underlying neural circuitry, however, is different (Hausen and Strausfeld, 1980). It is not necessary that movement and position computation occurs in different "channels" (eg. 1-input and 2-input channels). Position information could also be obtained for example at the output of the movement computation "box". The genetic dissection of the nervous system could be an appropriate tool to determine to what extend these two basic computations are executed independently.

In the following a selection method is described which is based upon the fixation response. It is the purpose of this selection to search for mutants with abnormal or missing fixation response, but otherwise normal visual response. From the existence of mutants deficient in their fixation but normal in their optomotor response, or vice versa, one may conclude that the two subsystems for position and for movement computation are working independently and are probably not controlled by exactly the same set of genes

during the development of the nervous system. Genetic dissection of one of the systems may facilitate the behavioural analysis and may be used as a convenient tool of reproducible microsurgery . The next step in understanding the orientation behaviour is the study at a lower level: the nerve cells and their wiring pattern as the basic constituents of behaviour. The most promising approach to this level in Drosophila is the Deoxyglucose method (Sokoloff, 1975) which is now also available for the investigation of the physiological activity of neurons in invertebrates (Buchner et al., 1979, Buchner and Buchner, in press).

## MATERIALS AND METHODS

Mutant selection:

Adult wild type "Berlin" males (less than 48 h old) were fed with 0.025 M ethylmethane sulfonate (EMS) according to the method of Lewis and Bacher (1968) and then mated to virgin attached-X-females. All F1 males carry a mutagenized paternal X-chromosome and each fly represents a differently treated sperm. The effectiveness of the mutagen was adjusted to about one lethal mutation per male X by controlling the amount of EMS fed such that a ratio of male to female progeny of 0.4 was reached. According to a Poisson distribution this value corresponds to an average of one recessive lethal per male X chromosome (Benzer, 1967). The male offspring was tested for behavioural defects in the "fixation Y-maze" which is described below. Putative mutants were cloned and the offspring was tested again. If the offspring also showed an abnormal fixation behaviour, i.e. a probability of less than 0.6 to approach the visual target, the strain was tentatively classified as fixation mutant.

Mutant strains and nomenclature:

All mutants with abnormal fixation behaviour have been given the designation "nof" (no object fixation). They are distinguished from each other by use of a capital letter (e.g. nofA, nofB, nofC, ...; nofA: Heisenberg, personal communication). Alleles of these mutants are further distinguished by superscripts (e.g. $nofC^{B1}$,

nofC$^{B2}$, nofC$^{B3}$, ...), usually beginning with the initial of the discoverer. Due to the special selection scheme, all mutations reported here are sex-linked. They are maintained either in a balanced strain on FM6, or as a homozygous stock, which has to be screened every 10 to 20 generations. Other mutants used, for example, in complementation tests are nbA, opm47, elf, omb$^{H31}$, omb$^{H53}$, tan$^{H24}$, nonA$^{H2}$, nonA$^{H17}$, X37, X61, X72, nofA$^{S71}$, nofA$^{S100}$, nofA$^{S129}$, nofA$^{S131}$, provided by M. Heisenberg.

The fixation maze:

To select mutants with abnormal fixation behaviour a special variant of the multiple-Y-maze (Hadler, 1964; Heisenberg, 1971a, b; Heisenberg and Götz, 1975) was used. The maze resembles "Galton's Board" and consists of 14 consecutive decision points at which the running fly has to decide to go either to the left or to the right (Fig. 1).

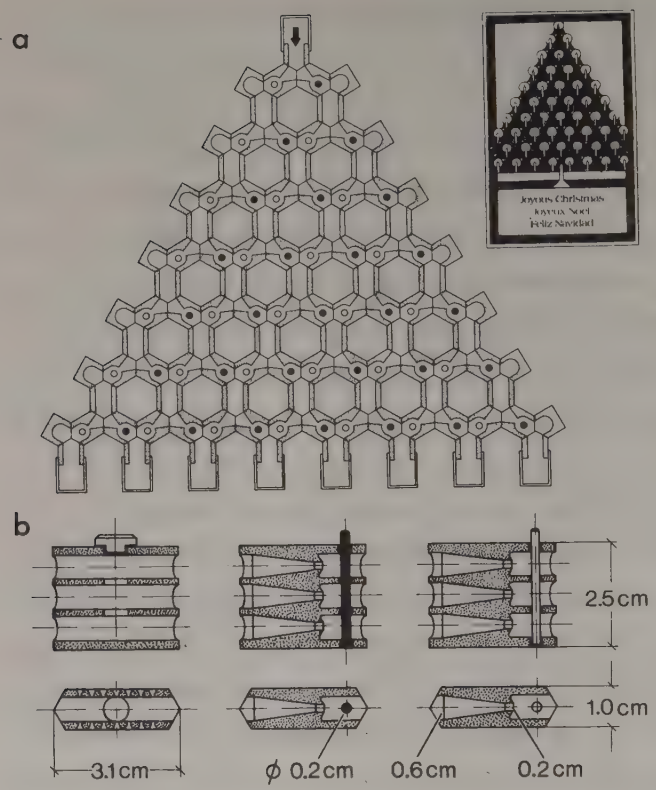


Figure 1

Principle of the multiple Y-maze used for the selection of fixation mutants. The simplified scheme comprises only 7 of the 14 choice levels used to increase the separation effect of a single choice element. (b) shows the 3 parts of which each of the 105 choice elements is composed. The "rectifying" nozzles in (b) direct the fly to the subsequent choice level and prevent the flies from running backward. The y-maze is placed horizontally.

(The design of the maze was "inspired" by a Christmas card from W.D. Kaplan.)

The decision of the fly is influenced by a tiny visual cue on one side at each choice point. This cue is a black stick of 0.2cmdiameter at a distance of 2.6 cm from the choice point in one of the two channels of a "unit cell". A similar but transparent stick is presented in the other channel. A circular segment of the sticks is seen by the fly behind the narrow ends of the translucent nozzles which are used to prevent the flies from running in opposite direction through the maze (Hirsch, 1959). The dark object on one side covers only 0.5 % of the visual field of the fly. This is obviously small enough to avoid significant photo-tactic effects. In a choice situation wild type flies will approach the tiny black spot with a probability p of approximately 0.75. To increase the separation effect the flies have to make 14 consecutive choices before arriving at one of 15 end cells where they are collected. Fig. 1b shows the building blocks of one of the 105 "unit cells" of which the maze consists. Since the end of a rectifier is a hole of only 0.2 cm, flies occasionally block the passage. To prevent clogging of the maze the flies are allowed to walk in 3 intercon-nected layers. The triplication of the maze increases the turnover. About 90 % of 300 flies starting from the empty culture cell in the upper Fig. 1a will run through the maze in about 16h. 5 % of the flies die in the departure vial, the other 5 % die later. A few flies stick in the nozzles.

The average distribution of 5740 wild-type (WT) flies in the end cells of the maze is shown in Fig. 2 (hatched columns). The best fit of the expectedly binomial distribution is obtained under the assumption that 75 % of the flies in a choice situation are actually running towards the small black target on the right (heavy contour line). Only 1 out of $3 \cdot 10^8$ flies are expected under these conditions in the end cell number 1 on the left. The actual ratio is somewhat larger in Fig. 2. This is probably due to the variability of the fixation response (Bülthoff et al., in prep.) and to the fact that some of the tests are slightly biased to one particular side. To diminish lateral bias the black sticks and the translucent sticks were interchanged between different runs of the selection procedure. From the experiments with interchanged pattern positions the left-right asymmetry of the flies, or the maze, can be calculated. Only a very small bias towards the left was found which has been observed also in other maze paradigms (Murphey, 1965; Hay, 1975; Heisenberg and Götz, 1975).

Using Drosophila males carrying induced mutations on their X-chromosome the following selection scheme was applied. Flies collected from vial number 11 to 15 were discarded because of their apparently normal fixation behaviour. Flies from vial number 6 to 10 are possible candidates for a nof mutation. These flies

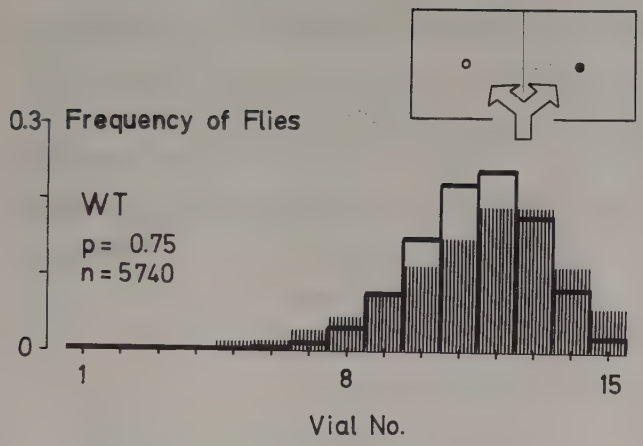


Figure 2

Frequency histogram of the distribution of 5740 normal fruit flies (wild type "Berlin", sex ratio 1:1) in the end cells of the fixation Y-maze (hatched columns). Between different runs the positions of the black and the transparent sticks were interchanged to eliminate lateral bias. The data are presented with reference to a position of the fixation target on the right. The calculated binomial distribution for p = 0.75 is shown by the heavy contour line. The inset illustrates the situation for a fly at each decision point. The visual object at the end of the channel covers only 0.5 % of the visual field of the fly.

were tested once again in the maze with interchanged pattern position. Vials number 1 to 5 contain most likely mutants with abnormal pattern orientation, because only 1 out of 3000 wild type flies is expected in these vials if the wild type fly is running with a probability of $p = 0.75$ towards the black target. These flies were mated to virgin attached-X females. The male offspring was tested again in the maze and mostly showed a binomial distribution with $0.4 < p < 0.6$. Homozygous females were made by two more crosses.

Automatic single fly tests:

The final screening for possible fixation mutants is carried out with single flies in a set-up allowing automatic recording of both the optomotor response and fixation response (Fig. 3). The test apparatus consists of: (a) a servo motor controlled cylindrical panorama to provide the visual stimulus; (b) a signal generator to control the rotatory movements of the panorama by a fixed programme of open-loop stimulation; (c) a small air-balanced dotted styrofoam ball in combination with an optical device to convert the locomotor activity of the stationarily walking fly into rotations of the ball which can be evaluated by automatic processing of the movements of the dots (Fig. 4).

Movement control of the visual panorama (a, b) was first described by Reichardt and Wenking (1969). The method for automatic registration of the optomotor response of walking flies (c) is adopted from Buchner (1976). By increasing the number of dots, and their optical magnification, the resolving power of this method has been improved by a factor of 5. This improvement is a prerequisite of successful closed-loop experiments.

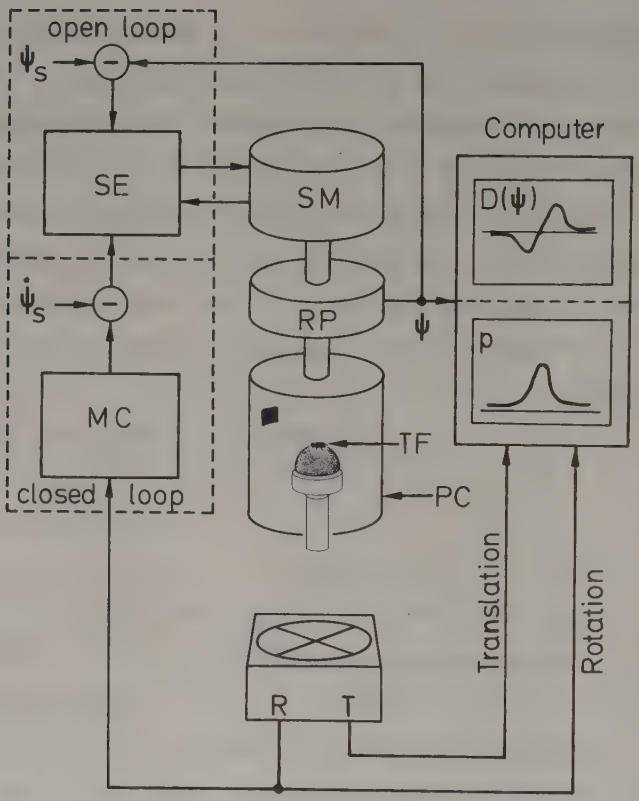


Figure 3

Simplified diagram of the set-up used for closed-loop and open-loop experiments. Under closed-loop conditions, the test fly (TF) controls the rotatory speed of the pattern cylinder (PC) by its own intended rotation, which is recorded by the device described in Fig. 4 (MC motor coupling, SM servo motor). The instantaneous pattern position is sent to the computer by means of a ringpotentiometer ( RP). Under open-loop conditions, the pattern position is controlled externally and the intended locomotion at different positions $\psi$ is evaluated by the computer. In this case, the ringpotentiometer is part of the feedback loop of the servo electronic (SE).

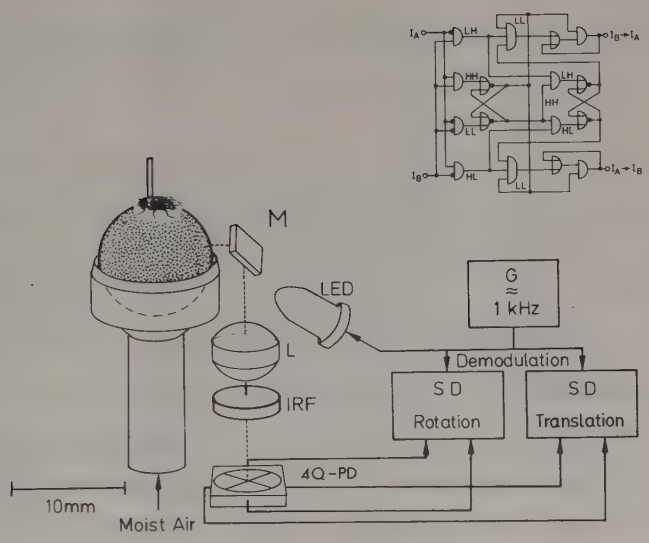


Figure 4

Registration of the intended locomotion of the tethered fly. (L) achromatic lens (f = 10 mm, 1:1.7); (LED) infrared high power light emitting diode (ME 7124, MONSANTO, Palo Alto, USA); (IFR) infrared filter (SCHOTT KG, Mainz, W.-Germany); (M) front silvered mirror; (4Q-P D) 4-quadrant photodiode (UDT PIN-SPOT-4D, TS-ELEKTRONIK, München, W.-Germany). The infrared illuminated spots on the ball are enlarged by lens L (10-fold) so that one spot on the ball covers about 75 % of the sensitive area of the 4-quadrant photodiode. The sequence of light-dark changes in the different areas of the detector is evaluated by a sequence detecting logic (SD). The LED is modulated (1 kHz) to obtain maximum peak power. Simultaneous demodulation of the optoelectrical signals diminishes the interaction of light signals from the rotating panorama. The inset shows the logic diagram of the sequence detector.

Automatic recording of the track of freely walking flies:

To investigate the behaviour of freely walking flies a fly to be tested is placed in the centre of the arena in Fig. 5, and is allowed to run freely for 200 s on a circular disk of 4.4 cm radius. The walking platform is surrounded (1) by a water-filled moat which prevents the fly from escaping, (2) by a light diffusing translucent plexiglass cylinder and (3) by four toroid-shaped dc-driven fluorescent lamps which illuminate the cylinder from outside. The luminance in the arena is in the order of 400 $cd/m^2$. The visual stimulus consists of two identical black rod-like objects, one on either side outside of the disc, which are seen against the white background of the surrounding cylinder. The area of the visual stimulus was chosen to resemble the stimulus in the Y-maze ($a = 0.15\ cm^2$). The path of the test-fly is recorded by a video system consisting of a 2/3" plumbicon camera (Philips LDH 26, Eindhoven, Netherlands) in combination with an object finder (Bülthoff et al., 1981). The XY-position of the fly on the disc is calculated by the object finder from the time between horizontal and vertical synchronisation, respectively, and the first occurrence of an object-induced video signal. The object finder delivers a sequence of plot pulses as long as the fly is moving within the annulus, scanned by the video system. The XY-coordinates are plotted on-line and recorded off-line on magnetic tape for later processing by

a 16-bit computer (PDP 11/34, Digital Equipment, Maynard, Mass., USA).

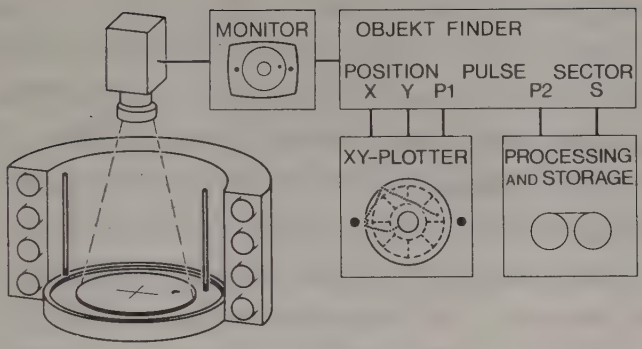


Figure 5

Test arena for automatic recording of the path of a freely walking fly with shortened wings. The fly is prevented from leaving the test arena by a water-filled moat. The XY-position of the fly on the walking platform is calculated by the object-finder from the time between horizontal and vertical synchronization, respectively, and the first occurrence of an object-induced video signal. The calculated position is recorded on-line by an XY-plotter or stored on magnetic tape for later evaluation.

Chromosome mapping:

The locus of the mutant gene within the one-dimensional chromosomal array can be determined by recombination mapping. The mutants were mapped on the X-chromosome using standard mapping crosses relative to four standard markers (followed by their symbol in brackets, and by their map position): yellow (y) 0.0, crossveinless (cv) 13.7, vermilion (v) 33.0 and forked (f) 56.7. More details in Lindsley and Grell (1968). The marker strain y-cv-v-f was provided by M.M. Green. To map the nof mutations one has to test each individual of the F2-generation from the mapping crosses for its fixation behaviour. This would be a very time consuming procedure taking at least 30 minutes per fly. To evade this difficulty all flies of the F2-generation were subjected to a simultaneous test in the selection machine. The distribution in the end cells is composed of two independent distributions, one of flies with normal fixation behaviour and another of those flies still carrying the fixation impairing gene on their X-chromosome. To calculate the location of the nof mutation one has to determine the number of mutant and wild type behavioural phenotypes linked to the different marker combinations. By a least square fit between the observed distributions for possible marker combinations, and the known distribution for wild type and mutant flies these figures could be estimated for each of the marker combination. It is obvious that this procedure lacks the

accuracy obtained by single fly screening. However, the genetic distances of the mutation from the loci of the markers appeared sufficiently consistent to attribute these mutations to particular regions in between any two of the markers of the X-chromosome. To obtain a better resolution other methods have to be used. For example the "segmental aneuploidy" technique, reviewed by O'Brienand McIntyre (1978), or the testing of lines of flies rather than single flies with a certain marker combination. To figure out "true" genetic distances the observed recombinant frequencies were corrected for multiple crossover according to standard techniques (Suzuki, 1976, p. 102).

Complementation tests:

The first problem arising with a newly isolated behavioural mutant is to determine whether this mutant is an allele of a previously known or unknown gene, respectively. A heterozygote of any two recessive mutations to be compared shows mutant behaviour whenever the mutant genes coincide, or normal behaviour in the absence of this coincidence. The normal behaviour is due to the complementation of the two defective genes by their normal counterparts in the heterozygote. This definition does not take into account intracistronic (intragenic) complementation. The 11 newly isolated nof mutants were tested for complementation against each other, and also against other mutants known for disturbed fixation behaviour: tan, $nonA^{H2}$, $omb^{H53}$,

X37, X72, $nofA^{S71}$, $nofA^{S129}$ (Heisenberg, 1972; Heisenberg and Götz, 1975; Heisenberg and Buchner, 1977).

Optical properties of the mutant eyes:

Two methods have been used to detect defects of the dioptric apparatus of the compound eyes in the living animal: (1) The inspection of the distal rhabdomere endings of large arrays of facets by optical neutralisation and antidromic illumination (Franceschini and Kirschfeld, 1971a). To compensate the optical convergence of the corneal lenslets, the whole eye is covered by a thin layer of a transparent nail polish having a refractive index close to that of the cornea. (2) The inspection of the deep pseudopupil formed by superposition of the virtual images of the rhabdomere endings of a number of ommatidia in the center of the eye (Franceschini and Kirschfeld, 1971b). Both methods show the characteristic trapezoidal arrangement of seven rhabdomere endings in a rhabdome, and are appropriate to study the migration of the screening pigment, a process controlling the light flux in the rhabdomeres (Franceschini and Kirschfeld, 1976). Mutant and wild type are mounted side by side under a microscope to achieve a fast comparison of the regularity of pattern, diameter and distance of the rhabdomere endings and of the cornea lenses.

Electro-retinography:

The flies were checked for defects in the periphery by measuring their electroretinogram (ERG). The light-induced ERG is mainly due to the electrical responses of the photoreceptors in the retina and the monopolar cells in the lamina of the fly's brain. The sustained on-response is attributed to the depolarisation of the receptor cells, whereas the cornea-positive on-transient and negative off-transient arise in the lamina (Goldsmith and Bernard, 1974; Pak, 1975). The flies were immobilized by ether or chilling and glued by the thorax to the tip of a needle using dental cement (Scutan , ESPE, Seefeld, W.-Germany). Legs, wings, proboscis and head were immobilized with the same glue to diminish the contamination of the ERG by muscle potentials. The respiratory movements of the abdomen were left unimpaired. The flies recovered from the anaesthesia after a few minutes and were kept in the dark for at least 30 minutes before the test. To record the ERG a glass microelectrode was filled with "Drosophila ringer" solution (0.13M-NaCl, 4.7M-KCl and 1.9mM-$CaCl_2$), and inserted just below the cornea. The reference electrode was inserted ventrally into the relatively soft thoracic-abdominal junction. The amplified signals from the electrodes were recorded in the memory of a signal averager (Histomat S, Deutsche Intertechnique, Mainz, W.-Germany). The resistance of the glass electrodes was between 50 and 150 M$\Omega$. For stimulation white light of a 150 W tungsten-iodine lamp was projected through a

magnetic shutter and heat filters onto a translucent diffusor in front of a hemisphere of a table tennis ball. This set-up provides a sufficiently uniform illumination inside of the hemisphere. The fly is placed into the center of the hemisphere with the inner surface in front of the test eye from which the ERG is taken. ERG depends upon the spatial and the spectral composition of the light stimulus. The uniform illumination of the visual field, therefore, facilitates the comparison of the responses of different flies (Hengstenberg and Götz, 1967; Heisenberg, 1971a, b). The maximum luminance of 1400 cd/$m^2$ was attenuated by different combinations of neutral density filters (Schott, Mainz, W.-Germany). In order to record the plateau of the negative cornea potential a comparatively long stimulus of 4 s was used. The interstimulus interval of 30 s was sufficient for dark adaptation under the conditions of the present experiments. The light programme was also recorded by the signal averager. The opening and closing time of the magnetic shutter was 0.75 ms.

Histology:

The proboscis of the ether-paralysed Drosophila was cut off by a vibrating knife in the fixative. The isolated head was maintained for 12 h in a solution of 2 % paraformaldehyde and 2.5 % glutaraldehyde in Millonig's phosphate buffer, containing 1.2 g D-glucose and 1 ml 1 % $CaCl_2$ per 100 ml (Millonig, 1961; Ribi, 1976). The tissue

was rinsed 5 times for 10 min in Millonig's buffer before being postfixed in a 2 % buffered $OsO_4$ solution for 30 min. The tissue was then dried in an acetone series and embedded in Araldite. Sections of 1.5 µmfor light microscopy were collected on a glass slide and stained with a 0.1 % toluidine blue solution.

## RESULTS

The orientation of flies towards the visual object in the multiple Y-maze was tested with available mutants known for partial or complete blindness or other defects in the processing of visual information. The results obtained by investigation of 24 different mutants are summarized in Fig. 6. As in Fig. 2 the hatched columns represent the relative number of flies in the end cells. The heavy contour line refers to the fitted binomial distribution. A probability of choice $0.5 < p < 1$, or a shift of the distribution to the right, indicates preferred orientation towards the object whereas a probability in the range $0 < p < 0.5$ is associated with antifixation, or orientation away from the object. The number of mutant flies in these experiments is given by n.

A few of the mutant strains show normal orientation effects as compared to the behaviour of the wild type in Fig. 2. These strains include the eyeless mutant ($\underline{ey}^2$) with rudimentary compound eyes and the mutants sevenless (sev) in which the inner rhabdomere 7 is missing,

the mutant with an extra lamina fibre (elf) (Heisenberg and Götz, 1975) and, surprisingly, also two of the S-mutants ($nofA^{S100}$, $nofA^{S131}$) which

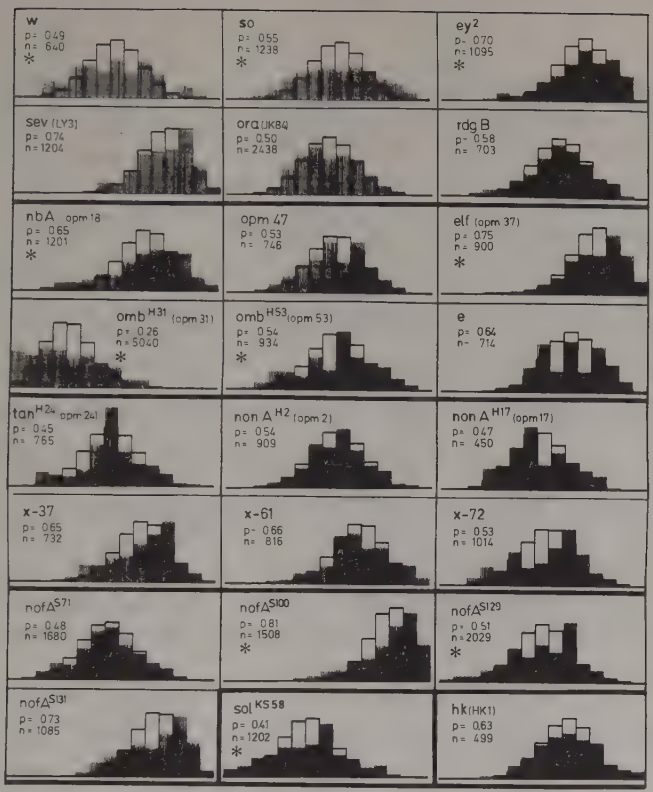


Figure 6

Frequency histograms of the distributions of 24 different mutants in the 15 end cells of the fixation Y-maze (hatched columns). The data are presented with reference to a position of the fixation target on the right. In each graph the probability p of making a turn to the right as calculated from the mean value of the distribution, and the number n of mutant flies tested is displayed. The calculated binomial distribution for this value of p is shown by the heavy contour line. The observed distributions which differ significantly ($\chi^2$ - test, $p < 0.001$) from the calculated binomial distribution are indicated by (*). In some cases the data are probably fitted better by a bimodal distribution. The figure is divided by the heavy frame lines into 6 different groups of mutants. From top to bottom: receptor mutants, optomotor blind mutants, ERG mutants, Heisenberg's "no object fixation" mutants nofA, small optic lobe mutant sol and hyperkinetic mutant hk. For more details about the mutants see text.

have been selected because of a defect in their attitude towards visual objects (Heisenberg and Wolf, 1979; Götz, 1980). The orientation effect is almost missing in the blind mutant sine oculis (so) (Götz, 1970), in the mutant white (w) lacking screening pigment (Götz, 1964, Hengstenberg und Götz, 1967) and a number of mutants of different optomotor blind (opm, omb) alleles (Heisenberg, 1972; Heisenberg and Götz, 1975) and mutants disturbed in the primary processes of phototransduction (x), no on-response (non), night blind (nb) and tan (tan) (Heisenberg, 1972; Heisenberg and Götz, 1975; Pak, 1975). The same holds for the hyperkinetik (hk) mutant (Kaplan and Trout, 1969) and the recently described small optic lobe (sol) mutant (Fischbach and Heisenberg, in press). Most surprising are the scores obtained in the behaviour of the optomotor blind mutant $omb^{H31}$ (Heisenberg et al., 1978), a mutant with severely diminished movement-induced course control response which is structurally impaired in the lobula plate giant neurones of the visual system. The flies of this strain avoid the visual object in the Y-maze. The avoidance reaction, or antifixation is remarkably strong ($p = 0.26$) and seems to be in contradiction to the almost normal fixation response obtained in other experimental paradigms. This result will be discussed later in connection with experiments of freely walking flies.

The disturbed pattern-induced orientation of the majority of available behavioural mutants in the maze allows

at least two interpretations: Either the "behavioural" genes interfere with a variety of different behavioural traits or the choices made by the fly in the maze depend on a variety of such traits. In either case we expect to find, by the selection procedure in the multiple Y-maze, some of the already available mutants and possibly some new ones.

Screening of a total of 15.000 flies resulted in 11 mutants with choice coefficients ranging from $p = 0.4$ to $p = 0.6$ (Fig. 7). To assay for eye defects and blindness their optics and their ERG were checked as described before. Most of the mutants (9 out of 11) are actually affected in their early visual processing: 3 showing disturbed optics and 6 abnormal ERG responses.

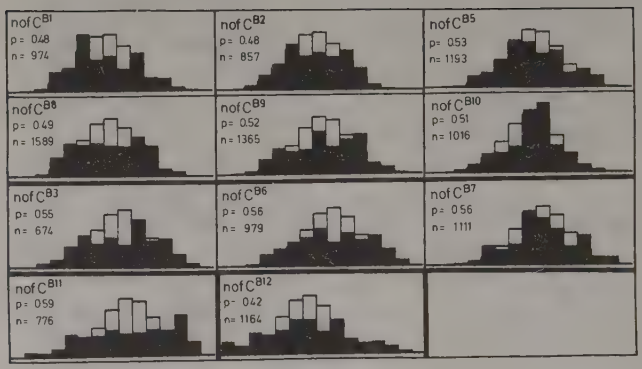


Figure 7

Frequency histograms of the distributions of the newly isolated "no object fixation" (nof) mutants in the end cells of the Y-maze (hatched columns). The data are presented as in Fig. 6. The figure is divided by the heavy frame lines into the complementation group of ERG mutants, the three different (no complementation) optic mutants and the two behavioural mutants $nofC^{B11}$ and $nofC^{B12}$ (no complementation).

Mutants affected in early visual processing.

Optic mutants:

In a first survey 3 of the mutants (nofC$^{B3}$, nofC$^{B6}$, and nofC$^{B7}$) showed different eye colour, darker and more brownish than the wild type. In semi-thin sections of the eye a reduced screening pigment can be observed (Fig. 8). These mutants also show irregularities in the pattern of the rhabdomere endings, which can be investigated by the optical neutralisation technique described before. In some of these mutants the endings are packed more closely than in the wild type. Very often the receptor endings are arranged in a more circular pattern which deviates from the normal trapezoidal arrangement. This, however, was not due to a missing receptor as in the mutant sevenless (sev). The number of receptors in a rhabdome was normal in all of the new mutants. Interestingly, inspection of the deep pseudopupil as described before was not possible in most of these mutants. Only a few showed a very blurred pseudopupil. According to Franceschini and Kirschfeld (1971a, b, 1976) this can be expected if the optical axes of the ommatidia within the region covered by the aperture of the microscope objective do not converge to a common intersection near the center of curvature of the eye.

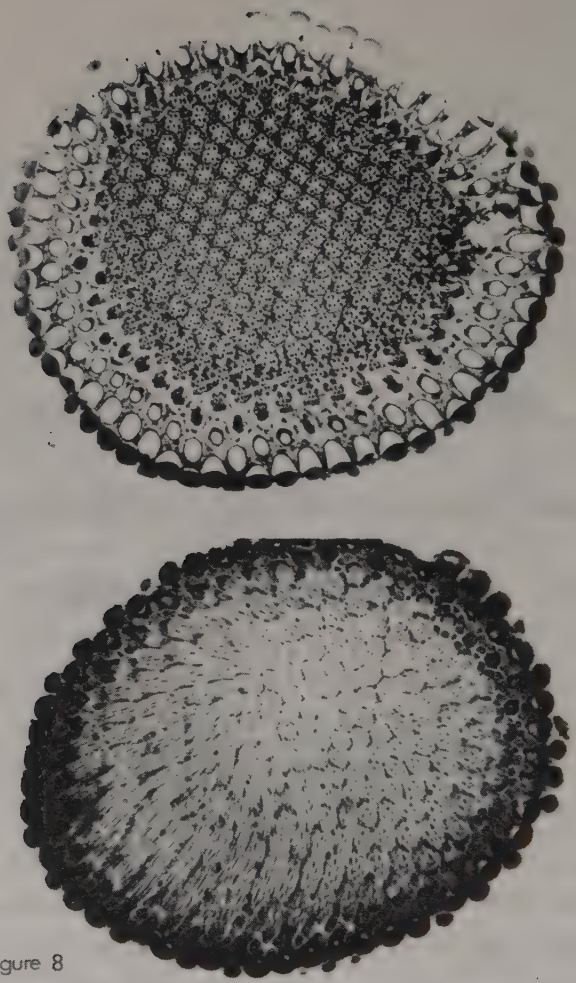

Figure 8

Tangential semi-thin (1.5 µm) sections through the retina of two mutant flies nofC$^{B6}$ (a) and nofC$^{B3}$ (b). Preparation as described in Methods. While the section in (a) cannot be distinguished from a corresponding section of a wild type fly, the sheath of screening pigment normally interlacing the retina in order to optically isolate neighbouring ommatidia is severely disrupted in the mutant nofC$^{B3}$ (b). These findings correspond to the appearance of the two intact individuals before histologic preparation: The fly in (a) had a normal eye colour and showed a normal "deep pseudopupil", while the eye appeared more brownish and a "deep pseudopupil" was not visible in the nofC $^{B3}$ mutant (b). Also, the dioptric apparatus of the mutant in (b) appears to be severely impaired. However, it is not yet clear to what extent fixation artefacts might contribute to this phenomenon.

In this case the virtual images of the rhabdomere endings cannot superimpose in the depth of the compound eye. Another reason for a blurred pseudopupil might be a displacement of the distal rhabdomere endings from the focal plane of the dioptric apparatus of the ommatidia. This can be tested by searching for real or virtual images of the antidromically illuminated receptor endings in individual intact ommatidia through adjustment of the focal plane of the microscope. If this plane was to be found distal to the cornea, it would mean that the receptor endings are located beyond the focal plane of the lens and the observed images would be real and inverted (as in the case of a slide projector). On the other hand, if the image plane was found proximally to the cornea (i.e. in the depth of an ommatidium), it would mean that the endings are located between the lenslet and its focal plane, in which case the observed images are virtual and erect (like an object observed through a magnifying lens). For the mutants $\underline{nofC^{B3}}$, $\underline{nofC^{B6}}$ and $\underline{nofC^{B7}}$ the latter case is true. This would suggest that the flies are unable to respond in the Y-maze, because the tiny pattern is blurred so much that it falls below the detection threshold. As shown in Fig. 6, the blurring of the pattern due to a 20 fold increase in stray light in the pigment-deficient mutant white (w)(Götz, 1964; Hengstenberg und Götz, 1967) obviously abolishes the object-induced orientation. However, the threshold is likely to decrease with increasing size of the pattern. The results,

therefore, do not exclude the detection of enlarged objects.

ERG mutants:

Since the ERG comprises the electrical responses of numerous receptor cells in the retina, and second-order cells in the lamina, it is frequently used as an unspecific indicator of the physiological and structural integrity of the peripheral stages of information processing in the visual system of mutants. The ERG of Drosophila can be decomposed into five components: A fast (1), and a slow (2), cornea-positive on-effect (Hengstenberg and Götz, 1967). Two cornea-negative sustained potentials (Pak et al., 1969), one with a short (3), the other with a long (4) rise and decay time, and finally a cornea-negative off-effect (5). These components are now fairly understood. The fast on- and off-responses arise in the lamina ganglionaris where most probably luminance adaptation and gain control take place. Most of the negative sustained potential is due to the receptor potentials of the retinula cells in the retina of the fly (Pak et al., 1969; Heisenberg, 1971a). Six of the 11 selected mutants with altered pattern orientation in the maze showed abnormal ERG responses. They belong to one complementation group but can be separated further into a group of mutants with abnormal transient responses (nofC$^{B1}$, nofC$^{B2}$, nofC$^{B5}$) and a group of mutants with abnormal time course of the receptor

potential (nofC$^{B8}$, nofC$^{B9}$, nofC$^{B10}$). In the first group the on-effect is slightly diminished whereas the off-effect is completely absent. The absolute sensitivity of the ERG is diminished by a factor of at least 1000 (nofC$^{B2}$ and nofC$^{B5}$ in Fig. 9a). In the second group (Fig. 9b) the return to baseline after light-off occurs with 2 - 5 s delay. There is no off-transient in all of these flies (Fig. 9). In many flies there is also no sustained response during light on. For some flies the potential is decreasing and in others it is increasing during the time period of stimulation (nofC$^{B9}$ in Fig. 9b). The decay to base line during the light stimulus is similar to that in the mutants of the transient receptor potential group (trp). The transient on-response was normal in most cases. The absolute sensitivity is reduced by a factor of at least 1000 for all mutants shown in Fig. 9. The ERG defects in the mutants of the present complementation group partially overlap with known ERG defects in mutants of different genotype. The main groups of ERG defective mutants belong to 5 different classes and are described in detail in a review by Pak (1975).

1) norpA cistron

The mutants of the norpA group are characterized by a complete, or nearly complete, absence of the ERG. So far, this has not been found in the nofC mutants.

2) tan, ebony, nonA, nonB cistrons

These 4 groups are similar both in ERG phenotype and optomotor behaviour. The salient feature of all four

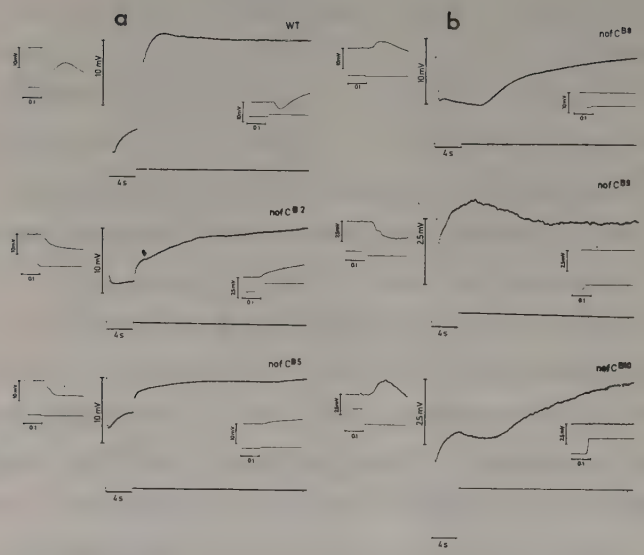


Figure 9

ERG responses of wild type (WT) and no object fixation (nof) mutants to a light stimulus of 4 s duration. The maximum luminance of 1400 cd/m$^2$ was measured at the inner surface of a translucent hemisphere in front of the test eye from which the ERG was recorded. The insets to the left and to the right of the recorded potentials show the on- and off-transients at increased time resolution. Note that the off-response is missing in all mutants, whereas the on-response in most mutants is only slightly diminished. The mutants nofC$^{B1}$ (not shown), nofC$^{B2}$ and nofC$^{B5}$ belong to one complementation group. The defect responsible for the missing off-transient is probably localized in the lamina. The mutants nofC$^{B8}$, nofC$^{B9}$ and nofC$^{B10}$ (Fig.9b) belong to another complementation group. The mutation probably affects both the receptor cells in the retina (cornea-negative sustained potentials) and the lamina ganglionaris (cornea-negative transient potentials).

groups of mutants are that on- and off-transient of the ERG are either absent or very small in amplitude (Pak et al., 1969, 1970; Hotta and Benzer, 1969, 1970; Heisenberg, 1971a, b). In contrast, the nofC mutants are only affected in the off-responses. Moreover, the mutants tan and $nonA^{H2}$ (opm2) do not complement with any of the nof mutants. Ebony (e) is on the third chromosome. The locations of the mutations of nonA (52) and nonB (52.3 - 56) on the X-chromosome do not coincide with the locations of $nofC^{B1}$ and $nofC^{B2}$ (0 - 17).

3) Cosens-Manning mutant

The ERG responses of this mutant to stimuli of durations of less than 3 s are similar to the wild type responses. For stimuli of longer duration the receptor component (sustained, corneal-negative component) of the mutant ERG decays to baseline in a few seconds. The ERG responses of the nofC mutants to light stimuli of 4 s duration do not show this decline to baseline.

4) slrp

This mutant shows an abnormally slow return of the receptor component of the ERG to the baseline after the stimulus is turned off. The on- and off-transients are somewhat reduced. The off-transient is missing in all of the nofC mutants. Moreover, the locus of the slow receptor potential mutation slrp (51.4) is different from the locus of $nofC^{B1}$ and $nofC^{B2}$ (0 - 17).

5) rdgA and rdgB group

The two mutually complementing groups of mutants, rdgA and

rdgB, are characterized by small and delayed ERG responses (Hotta and Benzer, 1970; Heisenberg, 1971a). The amplitude is reduced by a factor of 5 - 50 (Heisenberg, 1971a). An age-dependent degeneration of rhabdomeres can be observed by histology (Hotta and Benzer, 1970). The ERG of the nofC mutants is not much reduced (Fig. 9). The rdgB mutants show only a minor fixation ability in the Y-maze. Moreover, the locus of rdgA (29) and rdgB (33.0 - 56.7) is different from the locus of $nofC^{B1}$ and $nofC^{B2}$ mutants (0 - 17).

Behavioural mutants:

Of the 11 selected mutants only $nofC^{B11}$ and $nofC^{B12}$ are not affected in early visual processing, as tested so far by optical and ERG techniques. These mutants differ significantly from the wild type in object-induced orientation (Fig. 7). That the orientation behaviour of $nofC^{B12}$ is disturbed can be seen already in the culture vials or, even better, in a larger box where the free flight behaviour can be observed. The mutants seem to turn more often than wild type but this has to be analyzed quantitatively. The impression one gets is that the $nofC^{B12}$ mutants are not able to maintain a straight course towards an object. In order to determine the origin of the defective behaviour, single flies of the isolated strains were tested under conditions of stationary and free walk, respectively.

Visual control of locomotion in stationarily walking flies:

The locomotor response of a stationarily walking fly to a moving pattern may be attributed to a response to the movement, and a response to the position, of a given pattern. The apparent size of the pattern was chosen in analogy to the black object in the maze, subtending about 0.5 % of the visual field of the test fly. It was moving horizontally around the fly at an elevation above the equator of 22° and at a speed of 2, 20, or 200°/s. The pattern was moving through alternating cycles in clockwise (cw) and counterclockwise (ccw) directions. The responses of the flies to the movement are functions of the position $\psi$ of the pattern and are denoted $R_{cw}(\psi)$ and $R_{ccw}(\psi)$, respectively. It is always possible to decompose the optomotor response into (1) a direction-sensitive (ds) component which changes sign when the direction of the moving stimulus is inverted, and (2) a direction-insensitive (di) component which is invariant to such an inversion. These two components can be associated with movement and position computation, respectively. They can be derived from the responses to clockwise and counterclockwise movement in the following way (Geiger and Poggio, 1976). With respect to the right eye the direction-sensitive and direction-insensitive components $R^r_{ds}$ and $R^r_{di}$ are given by

$$R^r_{ds} = R^r_{cw} - R^r_{ccw}$$

$$R^r_{di} = R^r_{cw} + R^r_{ccw}$$

Similar relations are valid for the left eye. Under the assumption of bilateral symmetry of the fly, eye-independent quantities may be defined by

$$R_{ds} = 1/2\ (R^r_{ds} + R^l_{ds}) = R_{cw} - R_{ccw}$$

$$R_{di} = 1/2\ (R^r_{di} - R^l_{di}) = R_{cw} + R_{ccw}$$

In an alternative decomposition the optomotor response may be represented by two eye-independent components elicited by front-to-back ("progressive") and back-to-front ("regressive") motion:

$$R_{prog} = 1/2\ (R^r_{cw} - R^l_{ccw}) = 1/2\ (R_{ds} + R_{di})$$

$$R_{reg} = 1/2\ (R^l_{cw} - R^r_{ccw}) = 1/2\ (R_{ds} - R_{di})\ .$$

$R_{ds}$ and $R_{di}$ may then also be written as

$$R_{ds} = R_{prog} + R_{reg}$$

$$R_{di} = R_{prog} - R_{reg}$$

It is clear that the two representations are equivalent from a phenomenological point of view. On the other hand, one of the two descriptions may turn out to be more appropriate if the neuronal mechanims underlying movement and position computation are taken into account (Poggio and Reichardt, 1980, Wehrhahn and Hausen, 1980). Conversely, analysis of genetic modifications of the responses in the two representations may provide hints to the specific

computational mechanisms involved. For these reasons both representations will be used in the following. In Fig. 10 the transient optomotor responses of wild type (WT) flies and mutants $\underline{nofC^{B11}}$ and $\underline{nofC^{B12}}$ are shown for clockwise (a) and, with inverted time scale, counter-clockwise (b) pattern movement (200°/s). As significant differences between males and females were not observed, only the pooled data are presented. The responses have been rearranged in (c) - (f) by combining the various components from the two eyes as described above. In (c) the responses are plotted with respect to progressive and regressive pattern motion ($R_{reg}$, $R_{prog}$). In (d) and (e) the decomposition into direction-sensitive and direction-insensitive responses $R_{ds}$ and $R_{di}$ is illustrated. In (f) the direction-insensitive component is plotted as the "attractiveness potential" U (Poggio and Reichardt, 1973b).

$$U(\psi) = \int_{-\pi}^{\psi} \left[ R_{di}(\psi') - R_{bias} \right] d\psi' ; \; R_{bias} = 1/2\pi \int_{-\pi}^{\pi} R_{di}(\psi') d\psi'$$

The following results are obtained from the decomposition of the optomotor response into progressive and regressive components (Fig. 10c). Wild type flies try to follow the progressive (front-to-back) movement of the pattern. Under the present stimulus conditions (small black pattern moving at 200°/s above equator) the corresponding response $R_{prog}$ does not depend on the position $\psi$ of the pattern in the fly's visual surround. The regressive response $R_{reg}$, on the other hand, strongly depends on the position of the

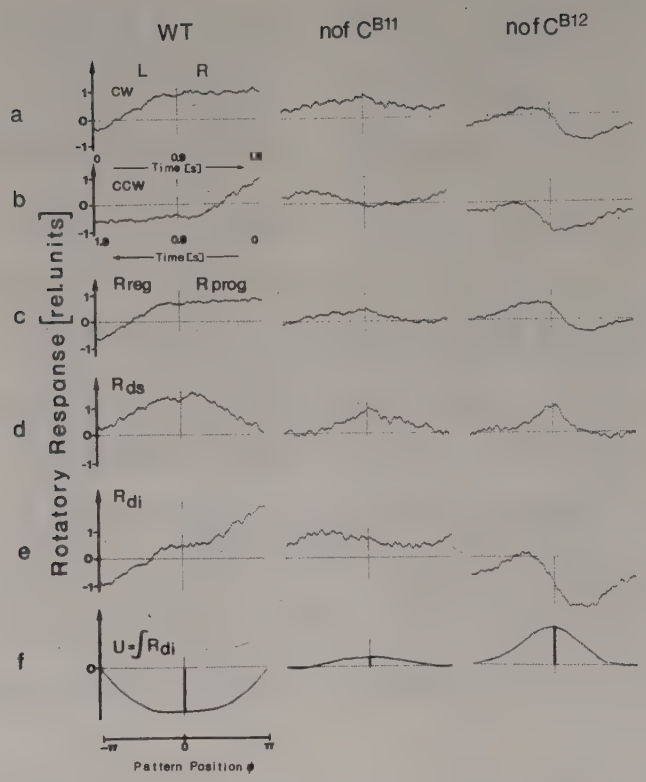


Figure 10

Transient optomotor responses of Drosophila to a small pattern (5 by 5°) moving 22° above the equator of the fly's eyes at 200°/s in alternating clockwise (cw) and counterclockwise (ccw) directions. Note the inverted time scale in (b). Positive responses reflect clockwise turning tendencies of the flies. The rotatory responses of wild type (WT) and no object fixation mutants nofC$^{B11}$ and nofC$^{B12}$ are rearranged in (c) - (f) by combining responses from left (L) and right (R) eye as described in the text. Each curve represents the average of 290000 - 430000 sweeps obtained from 5 - 6 females and 3 - 6 males.

target. At a lateral position of more than 90°, the response to regressive motion is negative, i.e., it is directed against the direction of the movement but towards the position of the pattern. The converse is true at lateral positions of less than 90°. In this case the fly tries to follow the direction of the regressively moving stripe, and its response is directed away from the position of the pattern. Under the same conditions the mutants behave quite differently. Their responses depend on the position of the moving pattern under progressive as well as regressive stimulation. The mutant nofC$^{B11}$ shows weak responses which are largest for the pattern moving in the frontal part of the visual field and fall off for more laterally located stimuli. With respect to progressive and regressive movement the responses are essentially symmetrical. The mutant nofC$^{B12}$, on the other hand, exhibits a pronounced asymmetry: the "following response" to regressive movement increases when the pattern moves from a lateral to a frontal position, whereas with progressive movement the "following response" decreases rapidly and even becomes negative (i.e. the fly turns against the direction of the movement) when the pattern is moving at a lateral position between $\psi$ = 30° and $\psi$ = 180°. Fig. 10d shows the dependence of the direction-sensitive component $R_{ds}$ on the position of the pattern. It is seen that $R_{ds}$ near $\psi$ = 0 is similar in all three strains, but, compared to wild type, decreases more rapidly with increasing $\psi$ in the mutant nofC$^{B11}$ and even more so in

nofC$^{B12}$. This leads to 2.5- and 3-fold smaller averages of the ds-responses, respectively. The direction-insensitive responses $R_{di}$, shown in Fig. 10e, and its bias-corrected integral, the potential U ($\psi$)(Fig. 10f), illustrate the attractiveness of the pattern to the flies. The negative potential of wild type reflects attraction to the position of the pattern while the mutant nofC$^{B12}$ tries to turn away from it (positive potential). Under closed-loop conditions these two potentials would lead to "fixation" in wild type and "antifixation" in the mutant nofC$^{B12}$. This might be compared to the responses of freely walking nofC$^{B12}$ mutants in the Y-maze, where they show a weak avoidance of the small black pattern ($P = 0.42$, Fig. 7). The small positive antifixation potential of the mutant nofC$^{B11}$ may not be significant.

In order to clarify the dependence of movement and position responses on the speed of the moving pattern, the above experiments were carried out with alternating sets of sweeps of 2, 20, and 200°. For clarity only the mean direction-sensitive and direction-insensitive responses, averaged over all pattern positions $\psi$, are shown in Fig. 11.

$$R_{ds} = 1/(2\pi)\int_{-\pi}^{\pi} R_{ds}\, d\psi$$

$$R_{di} = 1/\pi \int_{0}^{\pi} (R_{di} - R_{bias})\, d\psi$$

For WT flies both components are steeply increasing with

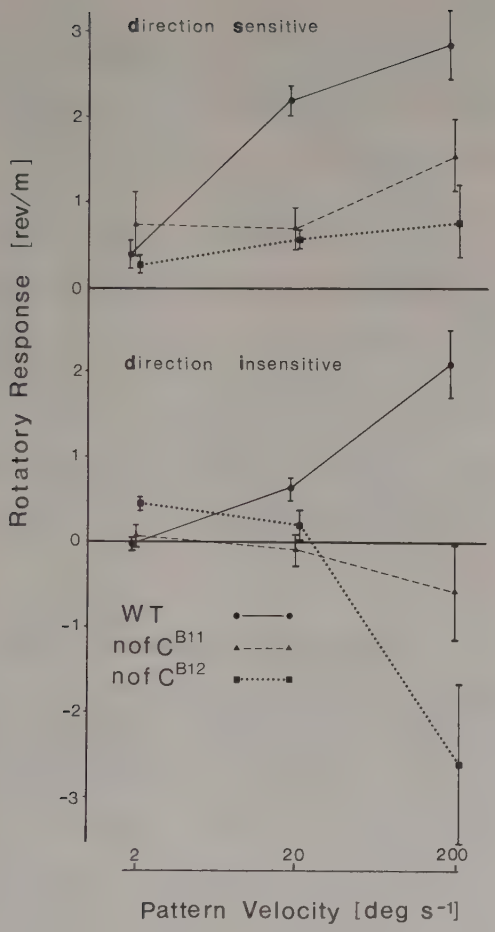


Figure 11

Average optomotor responses of Drosophila as a function of the pattern velocity. The direction-sensitive and direction-insensitive rotatory optomotor responses are plotted separately for wild type (WT) and no object fixation mutants nofC$^{B11}$ and nofC$^{B12}$.
Each point represents the average and the standard error of the mean of 8 - 12 flies (males and females).

increasing pattern velocity. This is not the case for the mutants. The direction-sensitive responses of both mutants are essentially flat, while the direction-insensitive response of nofC$^{B11}$ is not significantly different from zero at any of the three velocities tested. The direction-insensitive response of nofC$^{B12}$, however, is not only significantly negative at 200°/s (antifixation) as described above, but, most remarkably, changes sign as it is significantly positive at 2°/s (fixation). Thus it appears that genetic defects can modify the two components of the optomotor response rather independently. The reduced direction-sensitive responses cannot be attributed exclusively to a decrease in the resolving power of the mutant eyes. In Fig. 12 the direction-sensitive responses of wild type (WT) and the mutants nofC$^{B11}$ and nofC$^{B12}$ are shown for periodic gratings of different spatial wavelengths $\lambda$. Both mutants show small but significant negative responses for a pattern wavelength of 7.2°. This indicates that contrast transfer of the eye should be sufficient for small patterns to be detected. The zero crossing of the response curve is due to geometrical interference between the striped pattern and the periodic structures of the eye (Götz, 1964; Buchner, 1976) and is not significantly different from wild type. The characteristic sampling basis for movement detection is therefore most probably normal in these mutants. Evaluation of the curves shows a decrease in the direction-sensitive optomotor response by a factor of 3.2 in nofC$^{B11}$ and of

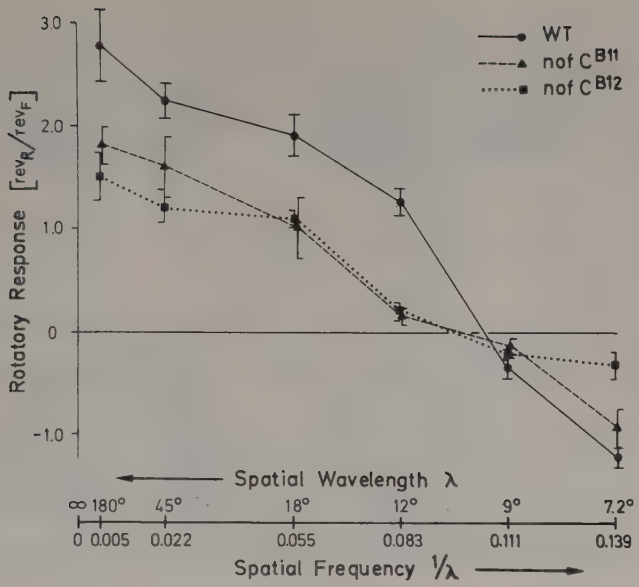


Figure 12

Average direction-sensitive rotatory optomotor response of Drosophila wild type (WT) and no object fixation (nofC$^{B11}$ and nofC$^{B12}$) mutants as a function of the spatial frequency ($1/\lambda$) of a striped drum. The "contrast frequency" was kept constant at $w/\lambda$ = 1 cps. The vertical extension of the pattern was about +/- 30°, the contrast of the pattern $\Delta I/\bar{I} \approx 0.95$. Luminance was about 80 cd/m$^2$. The rotatory response is plotted in units of rotatory revolutions ($rev_R$) per forward revolutions ($rev_F$) of the air-balanced ball in Fig. 4. Positive reactions indicate that the fly tries to follow the movement of the stripes. Each point represents the mean reaction and the standard error of the mean of 8 - 19 flies (males and females).

4.7 in nofC$^{B12}$. This is in good agreement with the results on the ds-responses for a small pattern in the upper visual field (Fig. 11).

Visual control of locomotion in freely walking flies:

To compare the orientation behaviour of wild type and mutant flies under more natural conditions the tracks of freely walking flies were recorded in the arena shown in Fig. 5. The two visual objects on either side of the centre of the arena create a situation similar to that of Buridan's ass in the early 14th century. Fig. 13 shows that the wild type actually behaves like this famous ass, running to and fro between the objects, sometimes for hours. The reversal of the course whenever the fly arrives at the moat in front of its target reveals a new aspect of the fixation behaviour. This fixation-antifixation dichotomy (Götz, 1980) is described in detail in a forthcoming paper (Bülthoff et al., 1980). It is tempting to reduce the contradictory orientation responses in different test situations (Y-maze, air-balanced ball, Buridan's paradigm) to a rivalry between the antagonistic behavioural traits of fixation and antifixation. This rivalry is likely to reconcile two remarkable discrepancies:
(1) The comparatively strong fixation response of the optomotor blind mutant omb$^{H31}$ (Heisenberg et al., 1978) in the arena which is in contrast to the conspicuous antifixation of this mutant in the Y-maze experiment (Fig. 6).
(2) The comparatively weak fixation response of a no-object-

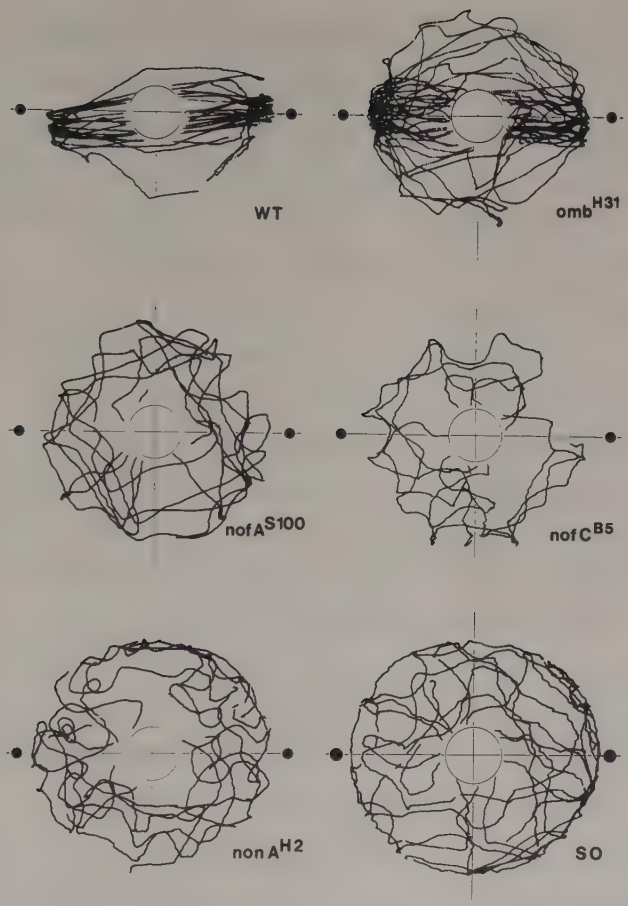


Figure 13

Traces of wild type and mutant Drosophila which are freely walking on an isolated disc of about 9 cm diameter. The wings are shortened to prevent flight. The paths of the flies were recorded for 200 s by the scanning device shown in Fig. 5. The automatic recording of the track is blanked out in the center, and at velocities below 0.1 cm/s. The dots on either side of the diagrams illustrate the diameter and position of the rod-like visual objects outside the disc on which the flies are walking. The apparent size of the black ends of the rods is equivalent to the apparent size of the black sticks to reflect the situation for the fly in the Y-maze in Fig. 1. For the description of the mutants see text.

fixation mutant nofA$^{S100}$ (Heisenberg et al., 1978; Heisenberg and Wolf, 1979) in the arena which is in contrast to the remarkably good fixation response in the Y-maze (Fig. 6). The orientation behaviour of the newly isolated nofC group produces low scores in both paradigms. In Fig. 13 the track of the nofC$^{B5}$ is plotted as an example for the behaviour of the whole group. Note, however, that the inter- and intra-individual variability in the orientation behaviour is far from being negligible. The orientation of the nof mutants with defective optics (nofC$^{B3}$, nofC$^{B6}$, nofC$^{B7}$) depends also on the apparent size of the visual object and, therefore, on the distance between fly and target. These flies may fixate the small object only in its immediate vicinity, where the target is still recognized. An example of weak fixation responses in both paradigms, the arena and the Y-maze, is represented by the mutant nonA$^{H2}$ (synonymous with opm2 or H2 in earlier work (Heisenberg, 1972)). This effect which occurs to a variable degree may be explained by selective suppression of course control responses. The responses to movement from back-to-front (regressive) are suppressed in this mutant to a variable degree for walking or flying mutants. The responses to movement from front-to-back (progressive) are suppressed when the mutant is walking. Note, however, that these responses may become remarkably normal under special conditions (Götz, 1980; Heisenberg, personal communication).

That the fly does not use other cues (e.g. odour) to detect the target is demonstrated by the completely blind sine oculis mutant so which has been checked for absence of photoreceptors (Götz, 1980).

## DISCUSSION

The selection technique described here has helped to isolate several most probably new mutants, supplementing already available genetic variations of the visual system of Drosophila. It is interesting that the new mutants evaded the screening for orientation blind mutants in other paradigms. Three results are worthwile to be mentioned in this context:

(1) A high percentage of the mutants show defects in the periphery of the visual system whereas only a minority of 2 out of 11 are likely to be central nervous system (CNS) mutants. The specific defects at the level of the receptors, however, may entail defects at subsequent levels of information processing.

(2) Some visual mutants did not show consistent defects of object-induced orientation responses under different fixation tests. A striking example is the strong anti-fixation of the optomotor blind mutant $omb^{H31}$ (Heisenberg et al., 1978) in the Y-maze and its normal fixation behaviour under stationary and free walking conditions (air-balanced ball and Buridan's paradigm). The free walking experiments in Buridan's paradigm revealed a fixation-antifixation dichotomy (Götz, 1980) which is not inherent in the present repertoire of optomotor responses. This dichotomy may be the cause for the discrepancy between antifixation in the Y-maze and fixation in Buridan's paradigm. A change in the relative weight of the fixation-

antifixation components might qualitatively alter the observed behaviour. The plasticity of the fixation behaviour is a quite common phenomenon. If monitored over a long time period (24 h) the fixation response of walking wild type flies is found to change from normal to antifixation behaviour (Bülthoff, unpublished). The variability of the pattern-induced fixation response between different flies is also much larger than it is the case for the movement-induced optomotor response. This variability is even higher for mutant strains due to the variable expressivity of the mutation. This can be seen for example in the deviation from a binomial distribution in the Y-maze. For many mutant strains the observed distribution is broader than the calculated binomial distribution. Individually tested flies taken from both ends of the distribution indeed show qualitatively different behaviour, i.e. fixation and antifixation.

These variabilities are of course influenced by the particular conditions of stimulation. The apparent discrepancy between some of the mutant fixation responses in different test situations is therefore easily comprehensible.

(3) Most of the already known mutants tested so far in the Y-maze show consistent defects in both, movement- and pattern-induced orientation behaviour. This coincidence raises the question whether or not specifically movement-blind or position-blind mutants actually exist. The main

goal of this work was the isolation of mutants which are disturbed in the pattern-induced orientation behaviour but show normal responses to movement stimuli. This goal has not been achieved, but, as so often, the negative result may bear some information. The newly isolated mutants combine defects in the pattern-induced orientation behaviour with deficient direction-sensitive optomotor responses. Conversely, this is true also for most of the available mutants selected for defects in the movement-induced optomotor response. This suggests that the pattern-induced and the movement-induced responses are connected either at the genetic level or at the neuronal level, or both. A partially common neural mechanism is feasible. In principle, visual responses to moving objects can be decomposed into a position dependent and a movement dependent component. At the neuronal level this decomposition might be implemented by the co-existence of purely direction-insensitive and purely direction-sensitive modules encoding position and movement, respectively. There is, however, at least another possibility: the decomposition into responses to progressive front-to-back movement ($R_{prog}$) and regressive back-to-front movement ($R_{reg}$) of the visual pattern. The position information would in this case be encoded in the difference $R_{prog} - R_{reg}$. Actually these decompositions are linear combinations of one another. From a phenomenological point of view it may be irrelevant which decomposition is assumed. This question requires an answer at the level of the underlying mechanism. Although the original description

of the fixation behaviour in Musca was outlined in terms of a progressive/regressive asymmetry (Reichardt, 1973), later experiments by B. Pick (1974, 1976) suggested that the position information was processed independently of the movement channel. In Drosophila, where evidence for independent processing of position information is missing, it has not been necessary to abandon the notation that the orientation response was depending on an asymmetry between progressive and regressive responses (Zimmermann, 1973; Götz, 1975). It is therefore natural to ask whether the data presented here favour a decomposition in terms of progressive and regressive channels. The transient responses to transient movement stimuli suggest that this might be the case. The mutants nofC$^{B11}$ and even more nofC$^{B12}$ seem to be affected mainly in their responses to progressive pattern motion. The opposite is seen in Heisenberg's optomotor blind mutant omb$^{H31}$. The transient responses of this mutant are qualitatively altered for regressive stimulation whereas the progressive response is only reduced (Bülthoff, unp.).The fact that in most cases the responses to progressive and regressive motion can be altered independently from each other suggests that the two postulated channels for the progressive and regressive responses are not connected, at least at the genetic level. However, one has to be careful with a generalization of the results obtained by the "genetic dissection" method. The independence of pro-

gressive and regressive channels holds only under the special stimulus conditions used here. Preliminary experiments for example show that the inversion of the progressive response of $\underline{nofC^{B12}}$ does not occur for monocular stimulation in a rotatory striped drum. In this case the mutant $\underline{nofC^{B12}}$ behaves like wild type, following the progressive moving stimulus. In this context one has to consider also the apparent contradictory behavioural results about movement and position channels obtained by Wehrhahn and Hausen (1980), Geiger (personal communication) and Brede (unp.).

It is quite likely that the simple schemes used to split the orientation behaviour in its basic components are still much too coarse as to faithfully reflect the responses of actual neural modules.

"We've got to keep coming up with something practical," Edison once remarked. "We can't be like those German scientists, who, as long as they keep getting their black bread and beer, are content to spend their whole lives studying the fuzz on a bee."

Thomas A. Edison

quoted in: physics today, June 1980

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# CURRICULUM VITAE

Am 18. 12. 1950 wurde ich als fünftes Kind des Günter Bülthoff und seiner Ehefrau Gertrud, geb. Meynen, in Zetel, Kreis Friesland, geboren. Von 1957 bis 1961 besuchte ich die Grundschule in Zetel, anschließend das neusprachlich-naturwissenschaftliche Gymnasium in Varel bis zum Abschluß durch die Reifeprüfung im Jahre 1970. Danach studierte ich Biologie in Berlin und Tübingen. Nach 8 Hochschulsemestern legte ich 1974 meine mündliche Diplomprüfung an der Eberhard-Karls-Universität in Tübingen ab. Anschließend fertigte ich am Max-Planck-Institut für biologische Kybernetik unter der Anleitung von Prof. K. G. Götz meine Diplomarbeit zum Thema "Nachweis einer Bewegungsillusion im visuellen System der Fruchtfliege Drosophila" an. Ab Juni 1975 arbeitete ich am gleichen Institut ebenfalls unter Anleitung von Herrn Götz an verhaltensphysiologischen und verhaltensgenetischen Untersuchungen am visuellen System der Fruchtfliege Drosophila.

Von meinen akademischen Lehrern sind insbesondere die Herren Professoren Götz, Grell, Hadeler, Kirschfeld, Krüger, Reichardt, Seyffert, Varjú, Weitzel, zu nennen.